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Figure 1.1

Recombinant bifunctional single-chain protein

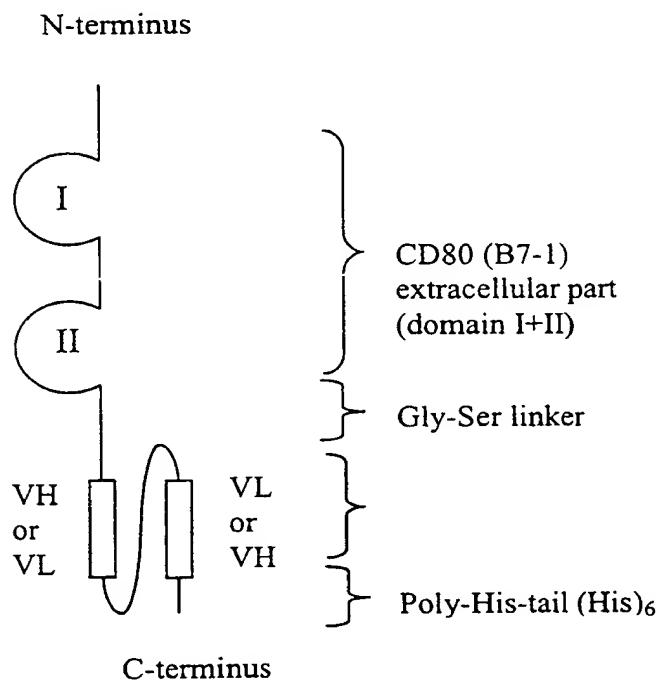


Figure 1.2 DNA-sequence designated CTI

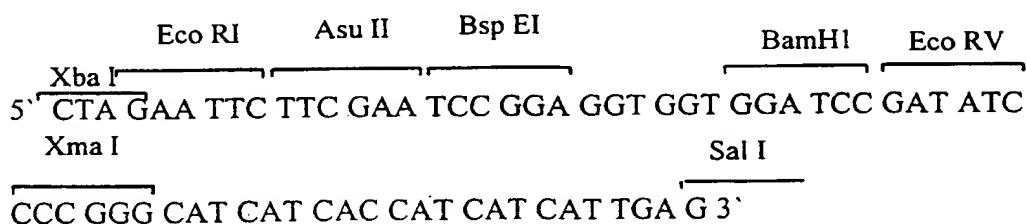


Figure 1.3 Design of various bifunctional CD80-scFv-constructs

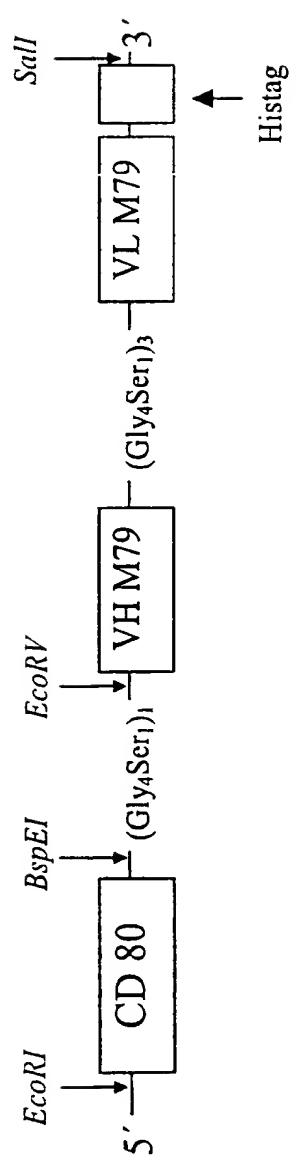
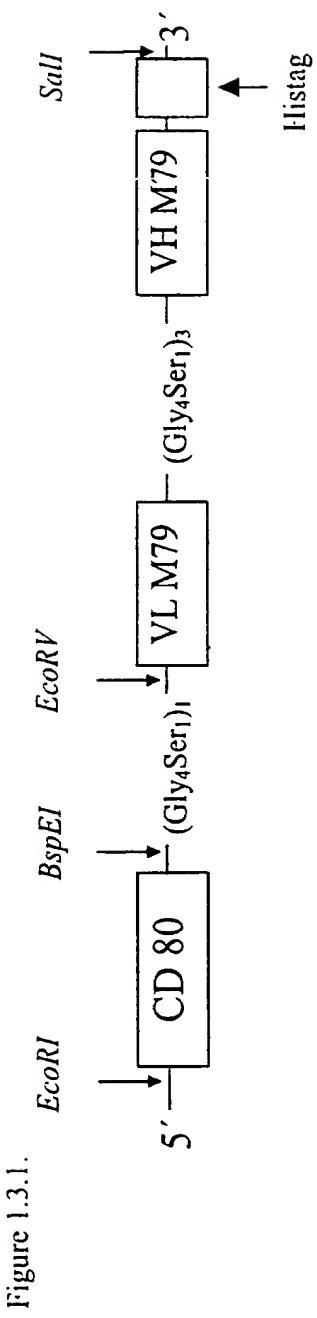


Figure 1.3.3.

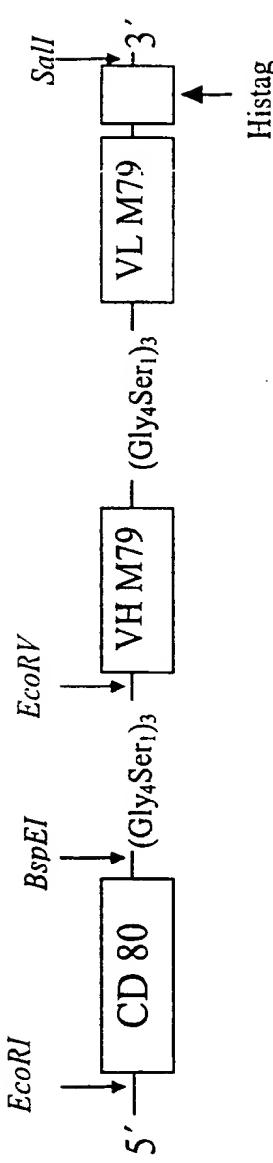


Figure 1.3.4.

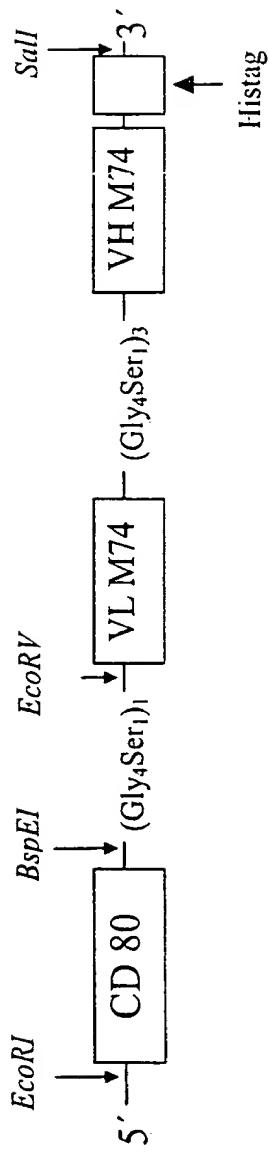


Figure 1.3.5.

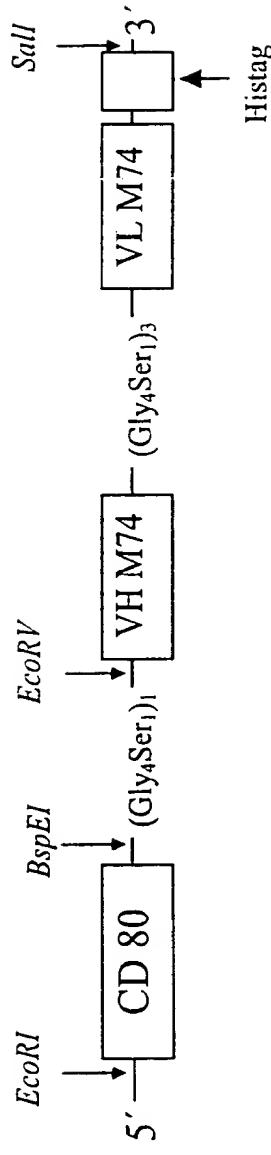


Figure 1.3.6.

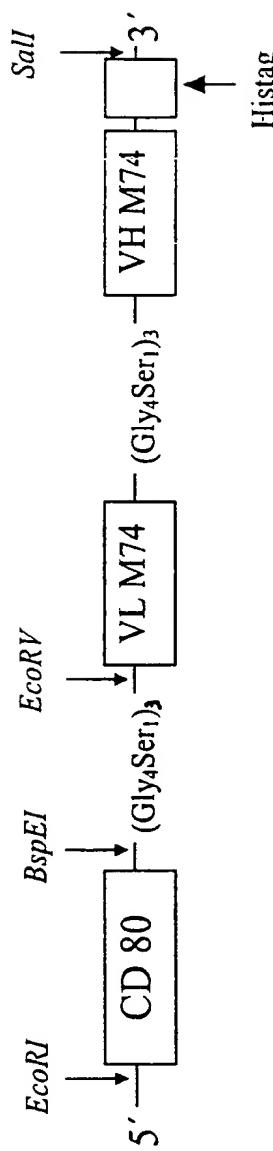


Figure 1.3.7

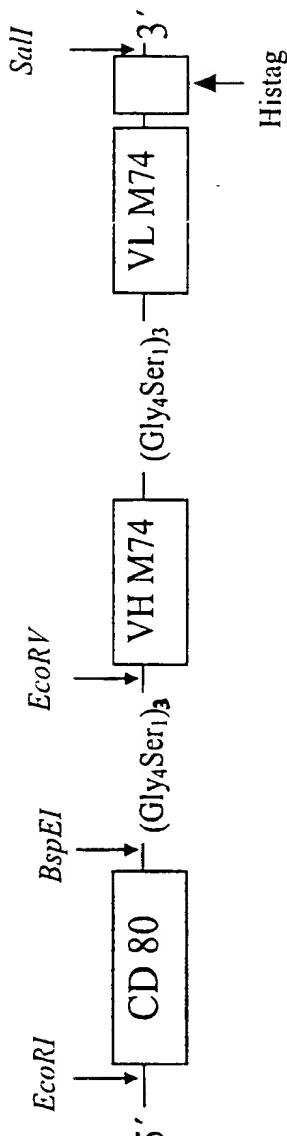


Figure 1.3.8.

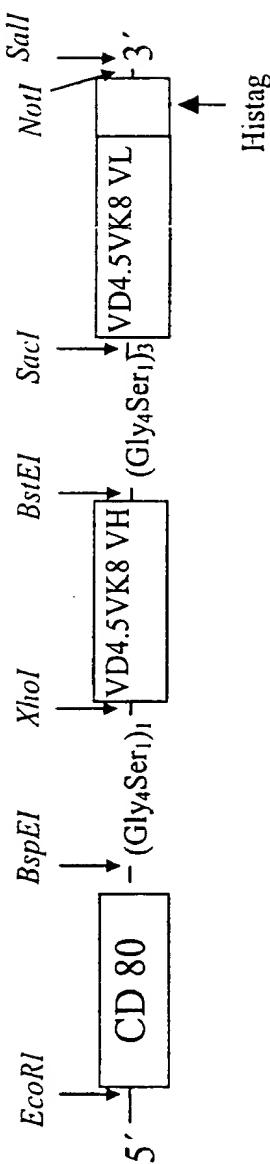


Figure 1.3.9.

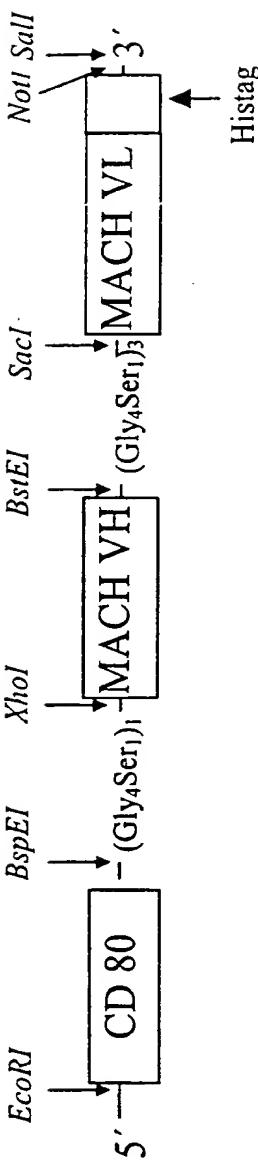


Figure 1.4

ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-His-tag

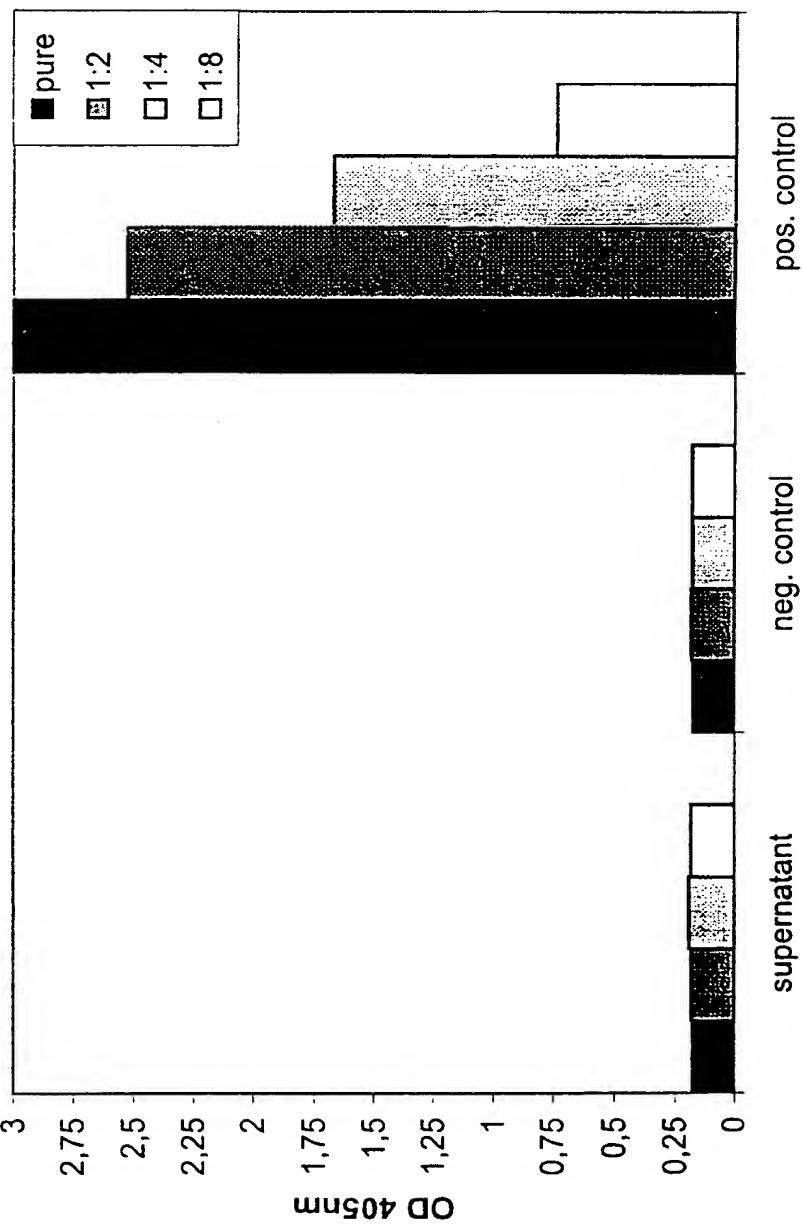


Figure 1.5

ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-CD80

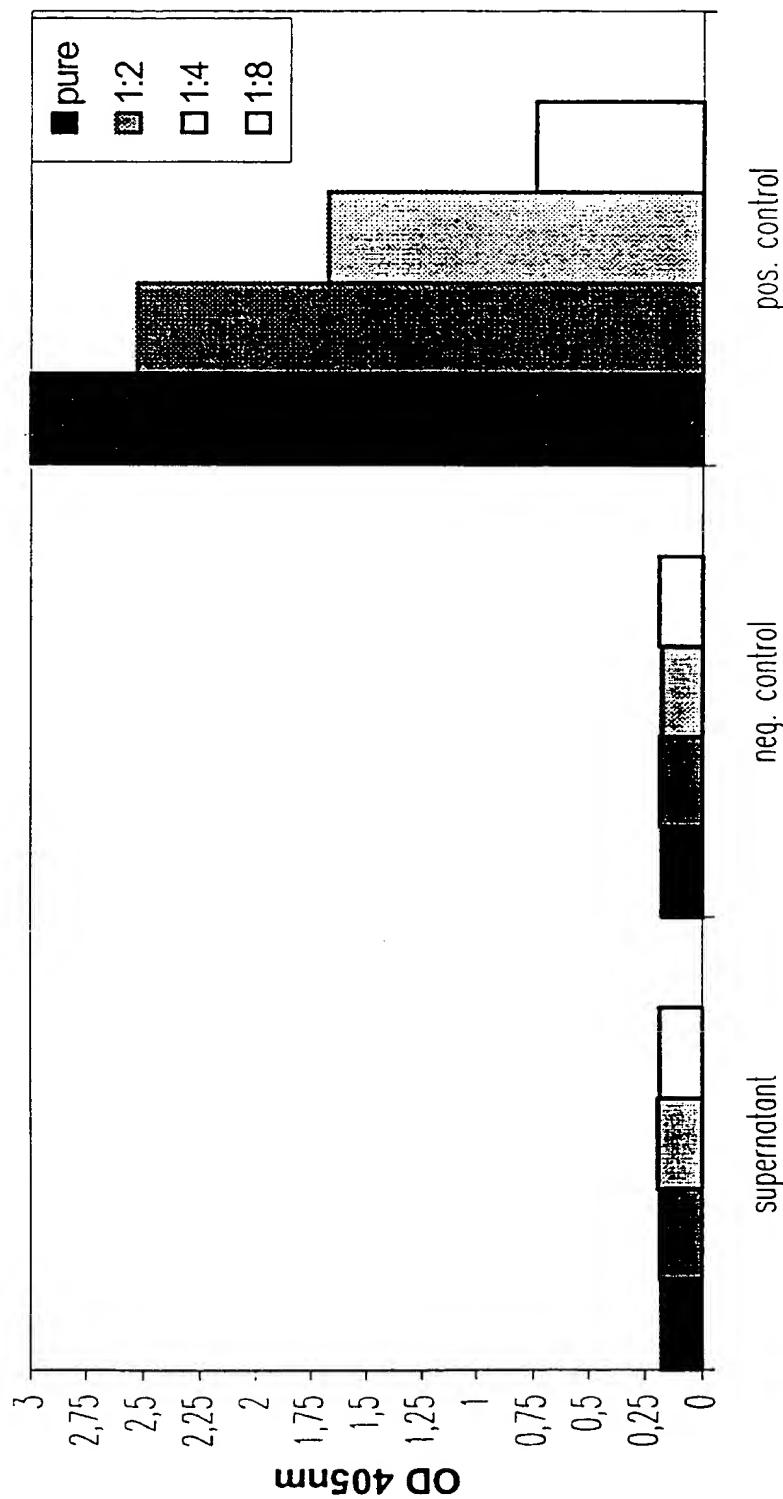


Figure 1.6

ELISA-analysis
CD80-M79scFv (VL/VH) with short linker
Detection: anti-His-tag or anti-CD80 (as indicated)

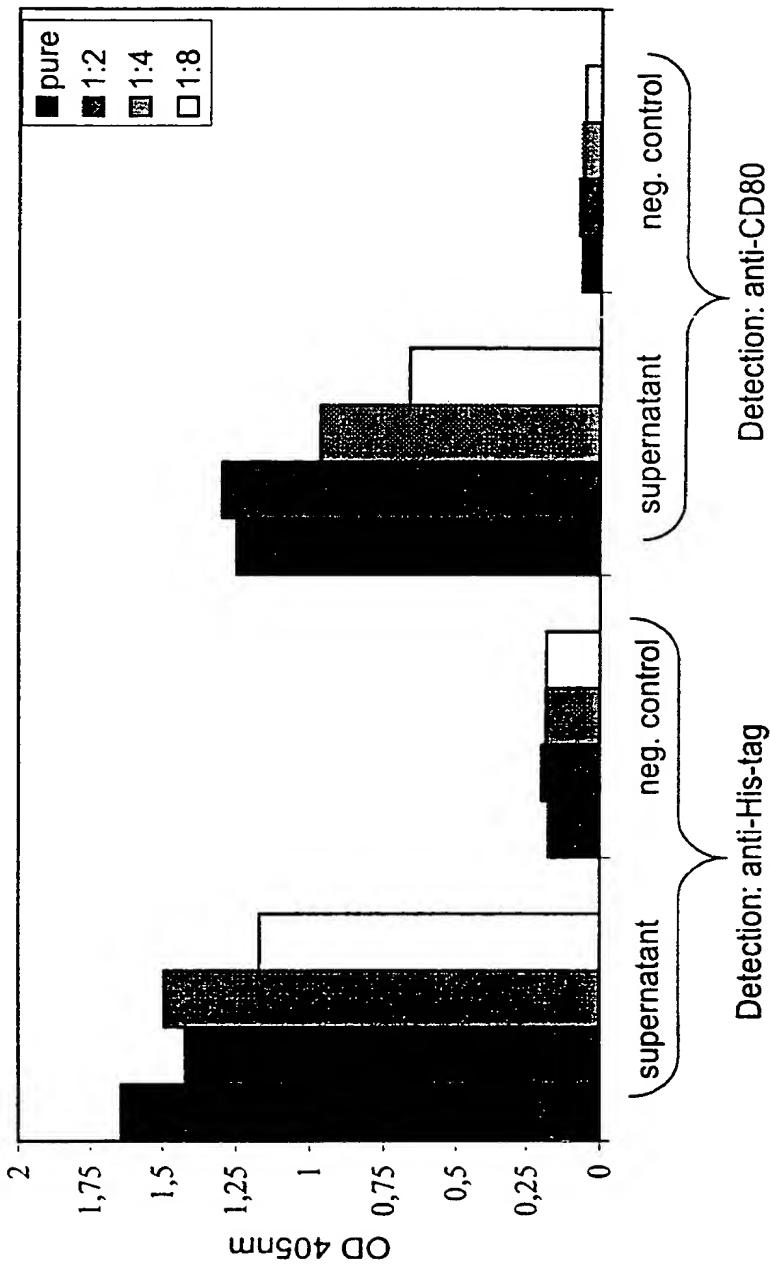


Figure 1.7

ELISA-analysis
CD 80-M 79 scFv (VH/VL) with short linker
Detection: anti-CD 80

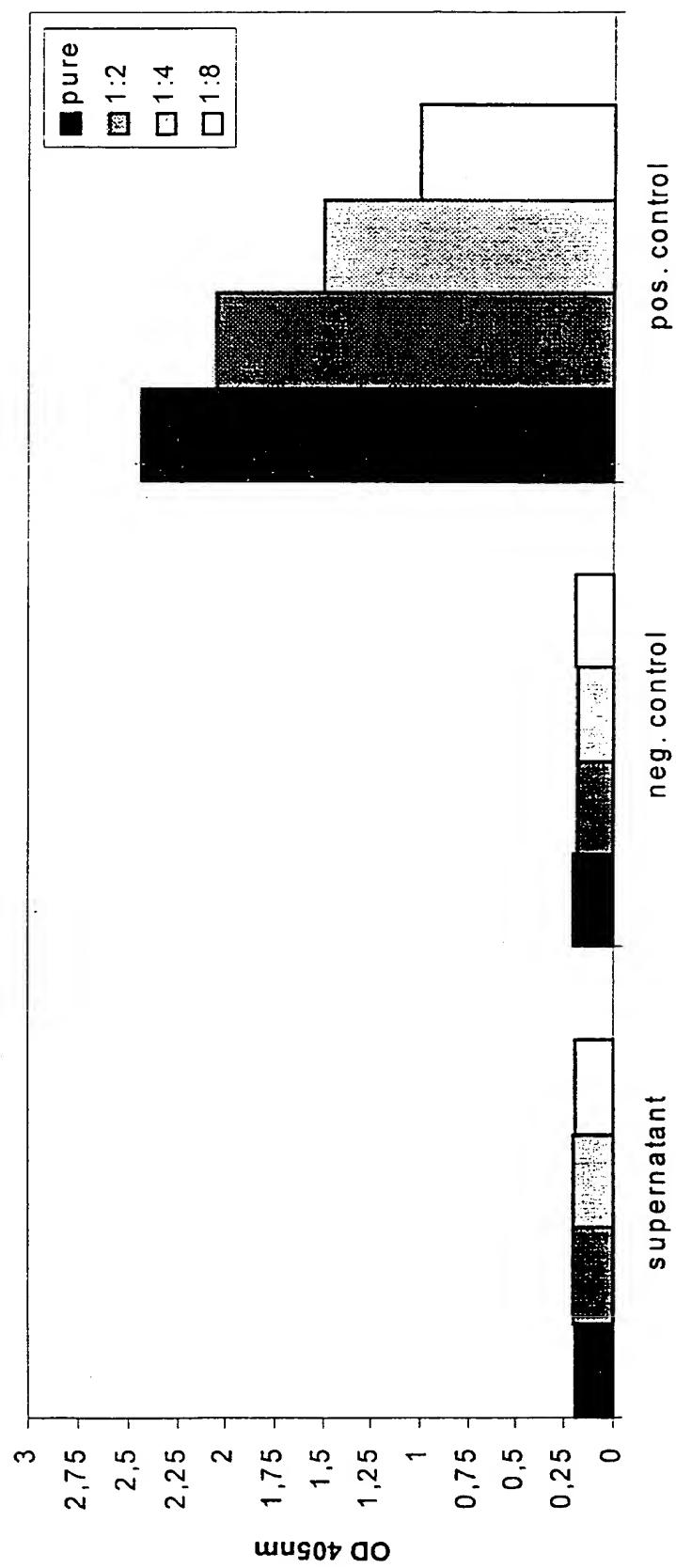


Figure 1.8 DNA-sequence of double-stranded oligonucleotide designated ACCGS15BAM

BspE1 Gly Gly Gly Ser Gly Gly Ser Gly Gly Gly
 5' pCC GGA GGT GGT TCC GGG GGT TCA GGT GGT GGT G 3'
 3' T CCA CCA CCA AGG CCC CCA CCT CCA AGT CCG CCA CCA CCTAG 5'
 Bam H]

Figure 1.9

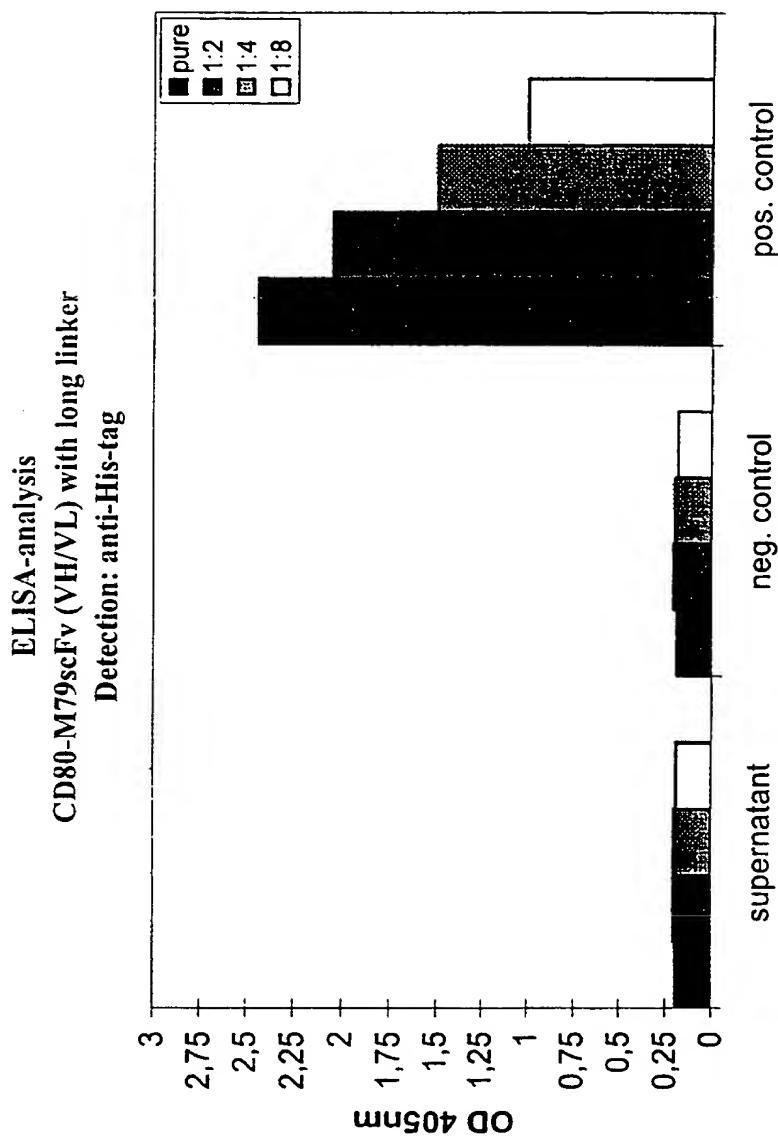


Figure 2.1

Elisa-analysis
CD80-M74 scFv with different linker lengths and either
VH/VL- or VH/VL-domain arrangement (as indicated)
Detection: anti-His-tag

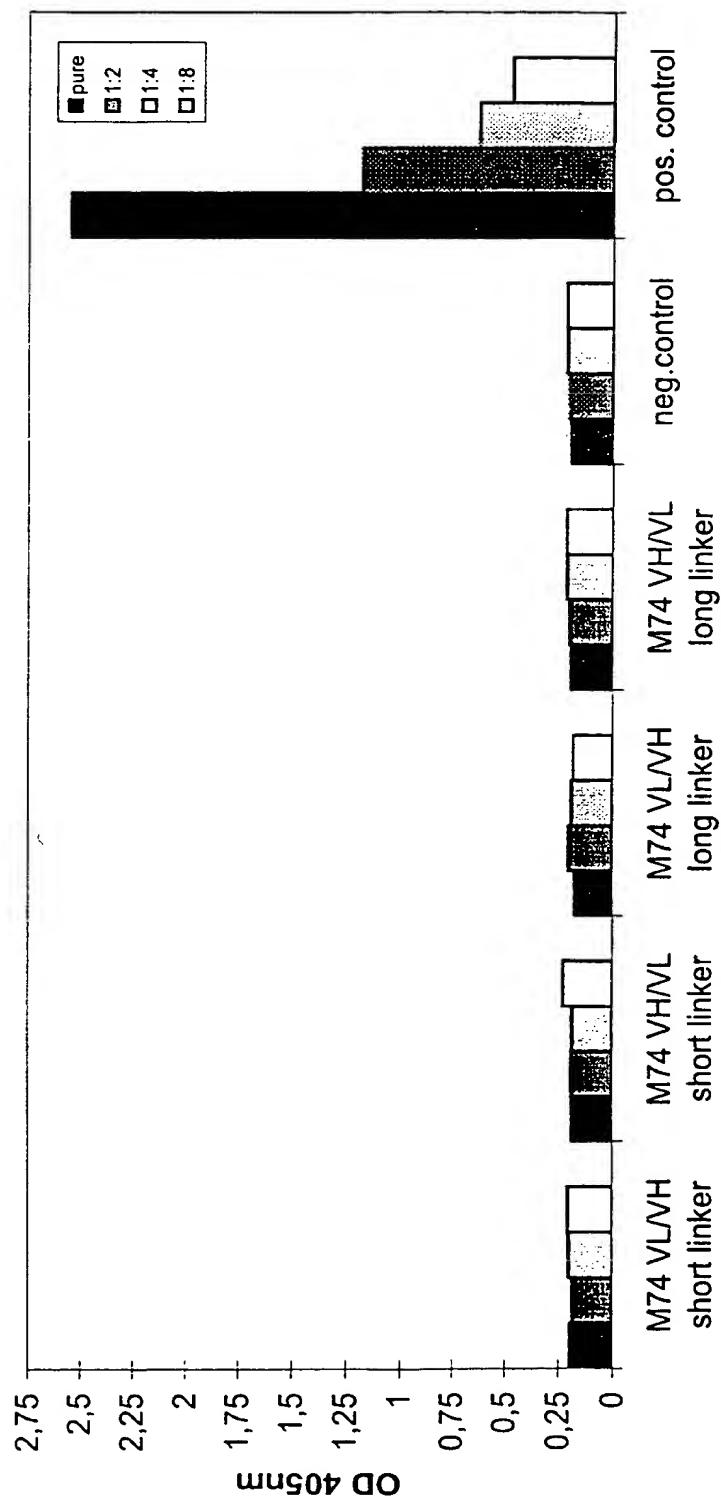


Figure 2.2

ELISA-analysis
CD80-M74 scFv with different linker lengths and either
VL/VH- or VH/VL-domain arrangement (as indicated)
Detection: anti-CD80

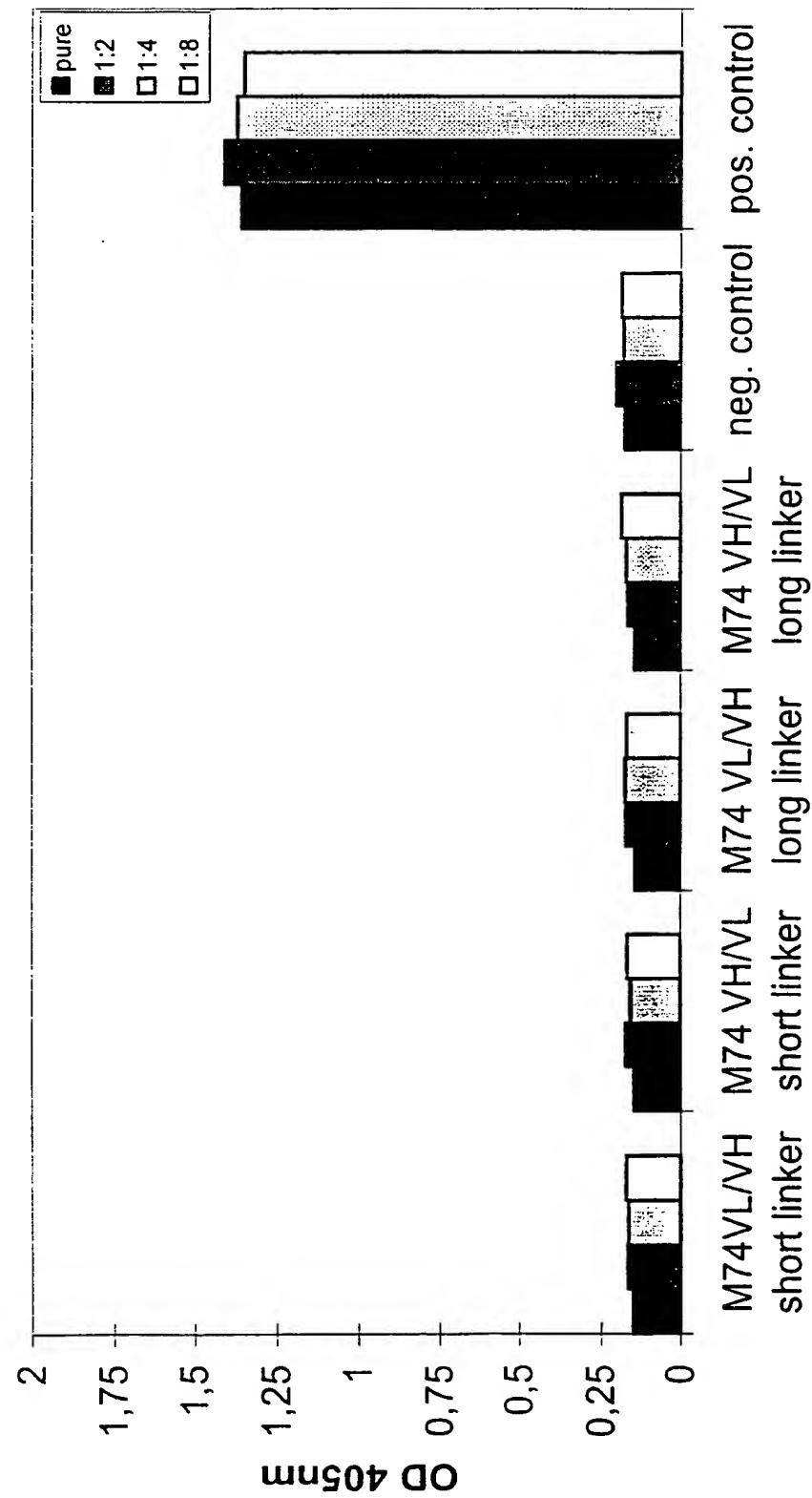


Figure 3.1

13/40

5'	GAG	GTG	CAG	CTG	CTC	GAG	TCT	GGG	GGA	GGC	GTG	GTC	CAG	CCT	GGG	AGG	TCC	CTG	9	18	27	36	45	54
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	E	V	Q	L	L	E	S	G	G	G	V	V	Q	P	G	R	S	L						
	63					72			81			90			99			108						
	AGA	CTC	TCC	TGT	GCA	GCC	TCT	GGA	TTC	ACC	TTC	AGT	AGC	TAT	GGC	ATG	CAC	TGG						
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	G	M	H	W						
	117					126			135			144			153			162						
	GTC	CGC	CAG	GCT	CCA	GGC	AAG	GGG	CTG	GAG	TGG	GTG	GCA	GTT	ATA	TCA	TAT	GAT						
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	V	R	Q	A	P	G	K	G	L	E	W	V	A	V	I	S	Y	D						
	171					180			189			198			207			216						
	GGA	AGT	AAT	AAA	TAC	TAT	GCA	GAC	TCC	GTG	AAG	GGC	CGA	TTC	ACC	ATC	TCC	AGA						
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	G	S	N	K	Y	Y	A	D	S	V	K	G	R	F	T	I	S	R						
	225					234			243			252			261			270						
	GAC	AAT	TCC	AAG	AAC	ACG	CTG	TAT	CTG	CAA	ATG	AAC	AGC	CTG	AGA	GCT	GAG	GAC						
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	D	N	S	K	N	T	L	Y	L	Q	M	N	S	L	R	A	E	D						
	279					288			297			306			315			324						
	ACG	GCT	GTG	TAT	TAC	TGT	GCG	AAA	GAT	ATG	GGG	TGG	GGC	AGT	GGC	TGG	AGA	CCC						
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	T	A	V	Y	Y	C	A	K	D	M	G	W	G	S	G	W	R	P						
	333					342			351			360			369			378						
	TAC	TAC	TAC	GGT	ATG	GAC	GTC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC							
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	Y	Y	Y	Y	G	M	D	V	W	G	Q	G	T	T	V	T	V	S						

TCA 3'

S

Figure 3.2

14/40

5'	GAG	CTC	CAG	ATG	ACC	CAG	TCT	CCA	TCC	TCC	CTG	TCT	GCT	TCT	GTG	GGA	GAC	AGA
	9	18	27	36	45	54												
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	E	L	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R
	63	72	81	90	99	108												
	GTC	ACC	ATC	ACT	TGT	CGG	ACA	AGT	CAG	AGC	ATT	AGC	AGC	TAT	TTA	AAT	TGG	TAT
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	V	T	I	T	C	R	T	S	Q	S	I	S	S	Y	L	N	W	Y
	117	126	135	144	153	162												
	CAG	CAG	AAA	CCA	GGA	CAG	CCT	CCT	AAG	CTG	CTC	ATT	TAC	TGG	GCA	TCT	ACC	CGG
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	Q	Q	K	P	G	Q	P	P	K	L	L	I	Y	W	A	S	T	R
	171	180	189	198	207	216												
	GAA	TCC	GGG	GTC	CCT	GAC	CGA	TTC	AGT	GGC	AGC	GGG	TCT	GGG	ACA	GAT	TTC	ACT
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	E	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T
	225	234	243	252	261	270												
	CTC	ACC	ATC	AGC	AGT	CTA	CAA	CCT	GAA	GAT	TCT	GCA	ACT	TAC	TAC	TGT	CAG	CAG
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	L	T	I	S	S	L	Q	P	E	D	S	A	T	Y	Y	C	Q	Q
	279	288	297	306	315													
	AGT	TAC	GAC	ATC	CCG	TAC	ACT	TTT	GGC	CAG	GGG	ACC	AAG	CTG	GAG	ATC	AAA	3'
	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	- - -	
	S	Y	D	I	P	Y	T	F	G	Q	G	T	K	L	E	I	K	

Figure 3.3

ELISA-analysis soluble VD4.5VK8-scFv-fragment Detection: anti-His-tag

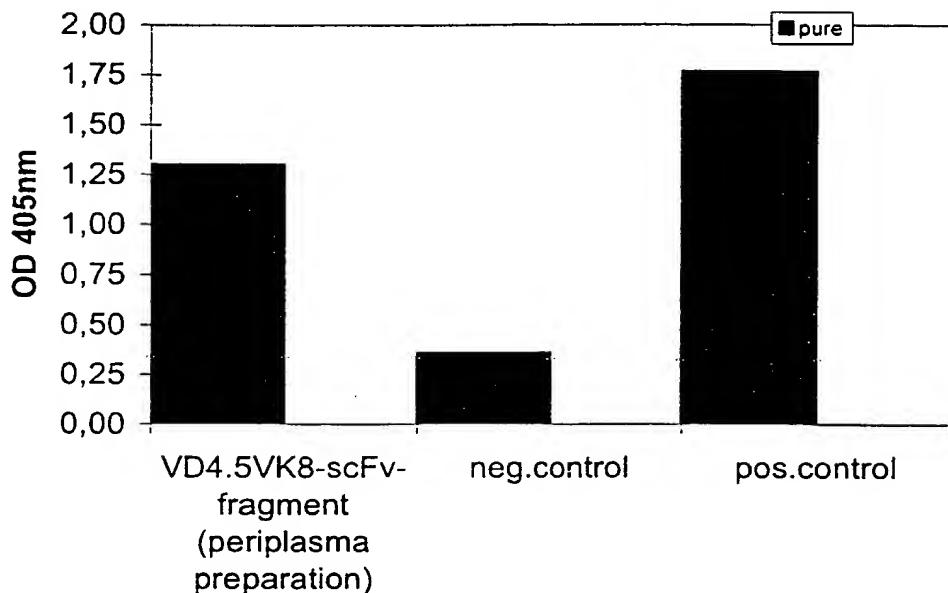


Figure 3.4 DNA-sequence designated L-F-NS3Frame

5' CCG CTC TAG AAT TCC ACC ATG GGA TGG AGC TGT ATC ATC CTC TTC TTG

 GTA GCA ACA GCT ACA GGT GTC CAC TCC GAC TAC AAA GAT GAT GAC GAT

 AAG GAT ATC TCC GGA GGT GGT AGC GCT ATT CCA TAT GGA CGT CCC

 GCT CGA GGT CGT CCA TCA TCA CCA TCA TCA CTG AGC GGC CGC TCT AGA

 GTC GAC CTC 3'

 EcoRI
 Eco RV Eco 47III NdeI
 XbaI Not I Xba I
 Sal I

Figure 4

ELISA -analysis
chimerized anti-17-1A antibody MACH
Detection: anti-human IgG

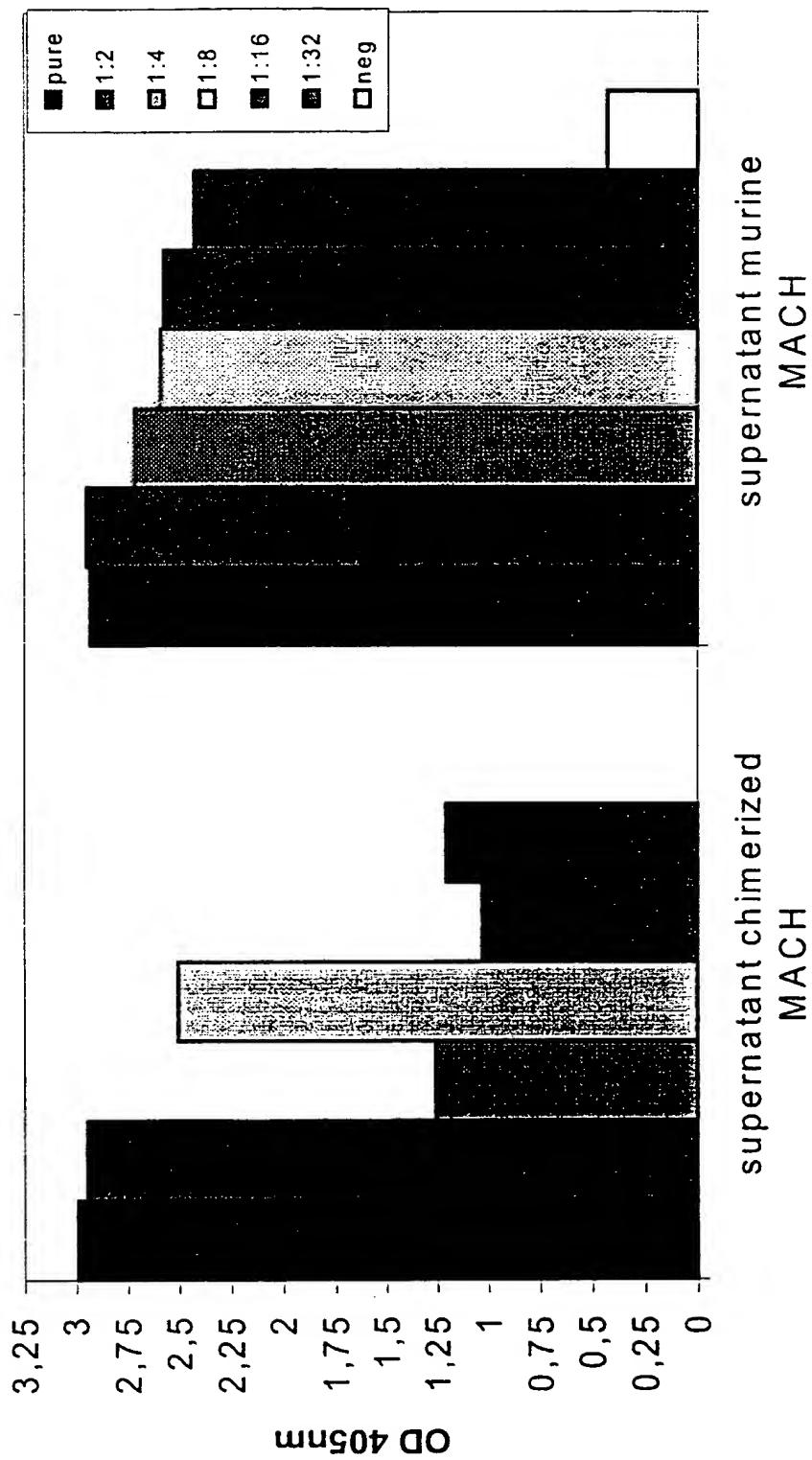


Figure 5.1

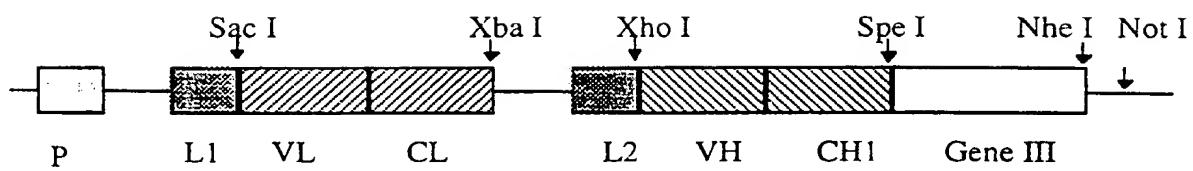


Figure 5.2 18 / 40

destroyed

Figure 5.3

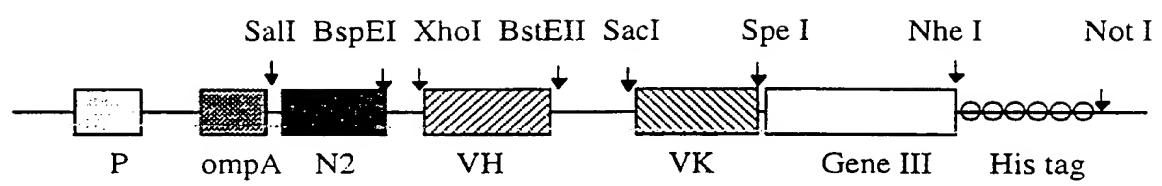


Figure 6.1

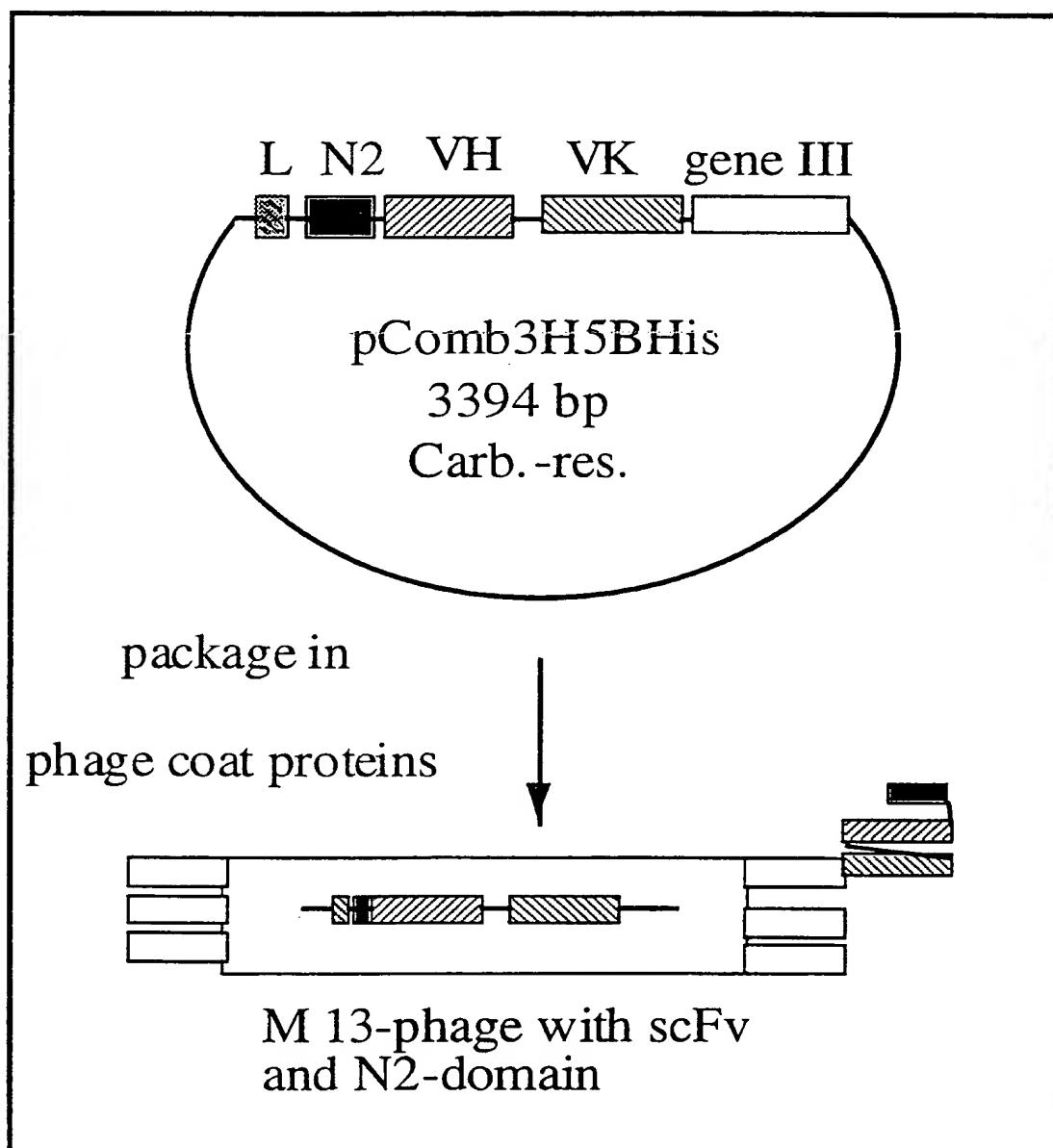


Figure 6.2

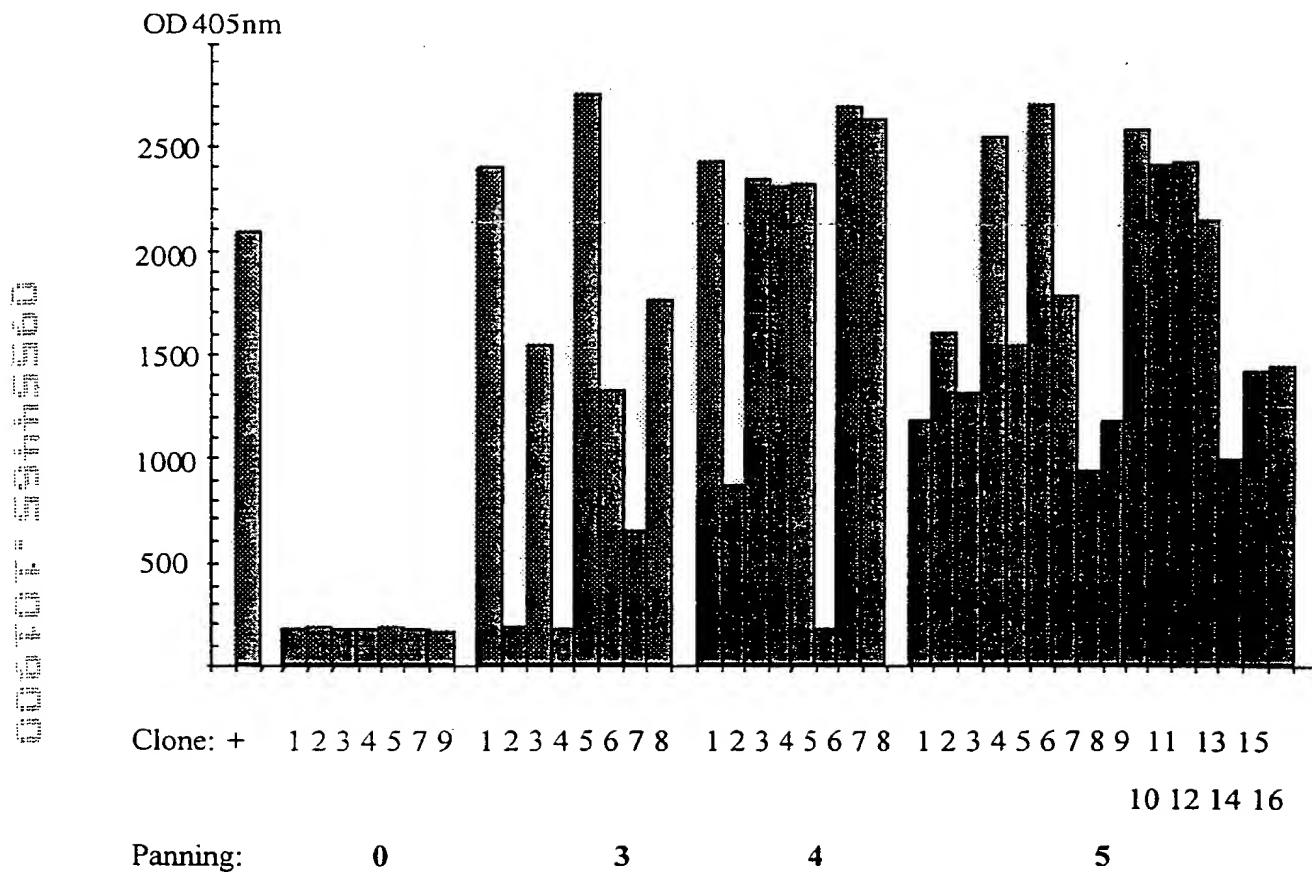


Figure 6.3

22/40

	9	18	27	36	45	54												
5	GAG	GTG	CAG	CTG	CTC	GAG	CAG	TCT	GGA	GCT	GAG	CTG	GTG	AAA	CCT	GGG	GCC	TCA
	E	V	Q	L	L	E	Q	S	G	A	E	L	V	K	P	G	A	S
	63					72			81			90			99			108
	GTG	AAG	ATA	TCC	TGC	AAG	GCT	TCT	GGA	TAC	GCC	TTC	ACT	AAC	TAC	TGG	CTA	GGT
	V	K	I	S	C	K	A	S	G	Y	A	F	T	N	Y	W	L	G
	117					126			135			144			153			162
	TGG	GTA	AAG	CAG	AGG	CCT	GGA	CAT	GGA	CTT	GAG	TGG	ATT	GGG	GAT	CTT	TTC	CCT
	W	V	K	Q	R	P	G	H	G	L	E	W	I	G	D	L	F	P
	171					180			189			198			207			216
	GGA	AGT	GGT	AAT	ACT	CAC	TAC	AAT	GAG	AGG	TTC	AGG	GGC	AAA	GCC	ACA	CTG	ACT
	G	S	G	N	T	H	Y	N	E	R	F	R	G	K	A	T	L	T
	225					234			243			252			261			270
	GCA	GAC	AAA	TCC	TCG	AGC	ACA	GCC	TTT	ATG	CAG	CTC	AGT	AGC	CTG	ACA	TCT	GAG
	A	D	K	S	S	S	T	A	F	M	Q	L	S	S	L	T	S	E
	279					288			297			306			315			324
	GAC	TCT	GCT	GTC	TAT	TTC	TGT	GCA	AGA	TTG	AGG	AAC	TGG	GAC	GAG	GCT	ATG	GAC
	D	S	A	V	Y	F	C	A	R	L	R	N	W	D	E	A	M	D
	333					342			351			360			369			378
	TAC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT	GGT	GGT	TCT	GGC
	Y	W	G	Q	G	T	T	V	T	V	S	S	G	G	G	G	S	G
	387					396			405			414			423			432
	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	GAG	CTC	GTC	ATG	ACC	CAG	TCT	CCA	TCT
	G	G	G	S	G	G	G	S	E	L	V	M	T	Q	S	P	S	
	441					450			459			468			477			486
	TAT	CTT	GCT	GCA	TCT	CCT	GGA	GAA	ACC	ATT	ACT	ATT	AAT	TGC	AGG	GCA	ACT	AAG
	Y	L	A	A	S	P	G	E	T	I	T	I	N	C	R	A	S	K
	495					504			513			522			531			540
	AGC	ATT	AGC	AAA	TAT	TTA	GCC	TGG	TAT	CAA	GAG	AAA	CCT	GGG	AAA	ACT	AAT	AAG
	S	I	S	K	Y	L	A	W	Y	Q	E	K	P	G	K	T	N	K
	549					558			567			576			585			594
	CTT	CTT	ATC	TAC	TCT	GGA	TCC	ACT	TTG	CAA	TCT	GGA	ATT	CCA	TCA	AGG	TTC	AGT
	L	L	I	Y	S	G	S	T	L	Q	S	G	I	P	S	R	F	S
	603					612			621			630			639			648
	GGC	AGT	GGA	TCT	GGT	ACA	GAT	TTC	ACT	CTC	ACC	ATC	AGT	AGC	CTG	GAG	CCT	GAA
	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	E	P	E
	657					666			675			684			693			702
	GAT	TTT	GCA	ATG	TAT	TAC	TGT	CAA	CAG	CAT	AAT	GAA	TAT	CCG	TAC	ACG	TTC	GGA
	D	F	A	M	Y	Y	C	Q	Q	H	N	E	Y	P	Y	T	F	G
	711					720												
	GGG	GGG	ACC	AAG	CTT	GAG	ATC	AAA	3'									
	G	G	T	K	L	E	I	K										

Figure 6.4

23/40

5'	GAG	GTG	CAG	CTG	CTC	GAG	CAG	TCT	GGA	GCT	GAG	CTG	GTA	AGG	CCT	GGG	ACT	TCA
	E	V	Q	L	L	E	Q	S	G	A	E	L	V	R	P	G	T	S
	63					72			81			90			99			108
	GTG	AAG	CTG	TCC	TGC	AAG	GCT	TCT	GGC	TAC	ACC	TTC	ACA	AGC	TAT	GGT	TTA	AGC
	V	K	L	S	C	K	A	S	G	Y	T	F	T	S	Y	G	L	S
	117					126			135			144			153			162
	TGG	GTG	AAG	CAG	AGA	ACT	GGA	CAG	GGC	CTT	GAG	TGG	ATT	GGA	GAG	GTT	TAT	CCT
	W	V	K	Q	R	T	G	Q	G	L	E	W	I	G	E	V	Y	P
	171					180			189			198			207			216
	AGA	ATT	GGT	AAT	GCT	TAC	TAC	AAT	GAG	AAG	TTC	AAG	GGC	AAG	GCC	ACA	CTG	ACT
	R	I	G	N	A	Y	Y	N	E	K	F	K	G	K	A	T	L	T
	225					234			243			252			261			270
	GCA	GAC	AAA	TCC	TCC	AGC	ACA	GGC	TCC	ATG	GAG	CTC	CGC	AGC	CTG	ACA	TCT	GAG
	A	D	K	S	S	S	T	A	S	M	E	L	R	S	L	T	S	E
	279					288			297			306			315			324
	GAC	TCT	GCG	GTC	TAT	TTC	TGT	GCA	AGA	CGG	GGA	TCC	TAC	GGT	AGT	AAC	TAC	GAC
	D	S	A	V	Y	F	C	A	R	R	G	S	Y	G	S	N	Y	D
	333					342			351			360			369			378
	TGG	TAC	TTC	GAT	GTC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT
	W	Y	F	D	V	W	G	Q	G	T	T	V	T	V	S	S	G	G
	387					396			405			414			423			432
	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	GAG	CTC	GTG	ATG	ACC
	G	G	S	G	G	G	S	G	G	G	G	S	E	L	V	M	T	
	441					450			459			468			477			486
	CAG	ACT	CCA	CTC	TCC	CTG	CCT	GTC	AGT	CTT	GGA	GAT	CAA	GCC	TCC	ATC	TCT	TGC
	Q	T	P	L	S	L	P	V	S	L	G	D	Q	A	S	I	S	C
	495					504			513			522			531			540
	AGA	TCT	AGT	CAG	AGC	CTT	GTA	CAC	AGT	AAT	GGA	AAC	ACC	TAT	TTA	CAT	TGG	TAC
	R	S	S	Q	S	L	V	H	S	N	G	N	T	Y	L	H	W	Y
	549					558			567			576			585			594
	CTG	CAG	AAG	CCA	GGC	CAG	TCT	CCA	AAG	CTC	CTG	ATC	TAC	AAA	GGT	TCC	AAC	CGA
	L	Q	K	P	G	Q	S	P	K	L	L	I	Y	K	V	S	N	R
	603					612			621			630			639			648
	TTT	TCT	GGG	GTC	CCA	GAC	AGG	TTC	AGT	GGC	AGT	GGA	TCA	GGG	ACA	GAT	TTC	ACA
	F	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T
	657					666			675			684			693			702
	CTC	AAG	ATC	AGC	AGA	GTG	GAG	GCT	GAG	GAT	CTG	GGA	GTT	TAT	TTC	TGC	TCT	CAA
	L	K	I	S	R	V	E	A	E	D	L	G	V	Y	F	C	S	Q
	711					720			729			738			747			
	AGT	ACA	CAT	GTT	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG	CTT	GAG	ATC	AAA	3'
	S	T	H	V	P	Y	T	F	G	G	G	T	K	L	E	I	K	

Figure 6.5

24/40

9	18	27	36	45	54
5' GAG GTG CAG CTG CTC GAG CAG TCT GGA GCT GCG CTG GTA AGG CCT GGG ACT TCA					

E	V	Q	L	L	E
63					72
					S
					81
					A
					A
					L
					V
					R
					P
					G
					T
					S
					108
GTG AAG ATA TCC TGC AAG GCT TCT GGA TAC GCC TTC ACT AAC TAC TGG CTA GGT					

V	K	I	S	C	K
117					126
					S
					G
					135
					Y
					A
					F
					T
					N
					Y
					W
					L
					G
					162
TGG GTA AAG CAG AGG CCT GGA CAT GGA CTT GAG TGG ATT GGA GAT ATT TAC CCT					

W	V	K	Q	R	P
171					180
					G
					H
					G
					L
					E
					W
					I
					G
					D
					I
					Y
					P
					216
GGA AGT GGT AAT ACT CAC TAC AAT GAG AGG TTC AGG GGC AAA GCC ACA CTG ACT					

G	S	G	N	T	H
225					234
					Y
					N
					E
					R
					F
					243
					252
					G
					K
					A
					T
					L
					T
					270
GCA GAC AAA TCC TCG AGC ACA GCC TTT ATG CAG CTC AGT AGC CTG ACA TCT GAG					

A	D	K	S	S	T
279					288
					A
					F
					M
					297
					Q
					L
					S
					S
					L
					T
					S
					E
					324
GAC TCT GCT GTC TAT TTC TGT GCA AGA TTG AGG AAC TGG GAC GAG CCT ATG GAC					

D	S	A	V	Y	F
333					342
					C
					A
					R
					L
					R
					N
					W
					D
					E
					P
					M
					D
					378
TAC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA GGT GGT GGT GGT TCT GCC					

Y	W	G	Q	G	T
387					396
					T
					V
					T
					V
					S
					S
					G
					G
					432
GGC GGC GGC TCC GGT GGT GGT TCT GAG CTC CAG ATG ACC CAG TCT CCA TCT					

G	G	G	S	G	G
441					450
					G
					S
					E
					L
					R
					N
					W
					D
					E
					P
					S
					486
TAT CTT GCT GCA TCT CCT GGA GAA ACC ATT ACT ATT AAT TGC AGG GCA AGT AAG					

Y	L	A	A	S	P
495					504
					G
					E
					T
					I
					T
					I
					N
					C
					R
					A
					S
					K
					540
AGC ATT AGC AAA TAT TTA GCC TGG TAT CAA GAG AAA CCT GGG AAA ACT AAT AAG					

S	I	S	K	Y	L
549					558
					A
					W
					Y
					Q
					E
					K
					576
CTT CTT ATC TAC TCT GGA TCC ACT TTG CAA TCT GGA ATT CCA TCA AGG TTC AGT					

L	L	I	Y	S	G
603					612
					S
					T
					L
					Q
					621
					Q
					H
					630
					639
GGC AGT GGA TCT GGT ACA GAT TTC ACT CTC ACC ATC AGT AGC CTG GAG CCT GAA					

G	S	G	S	G	T
657					666
					D
					F
					F
					675
GAT TTT GCA ATG TAT TAC TGT CAA CAG CAT AAT GAA TAC CCG TAC ACG TTC GGA					

D	F	A	M	Y	Y
711					720
					C
					Q
					Q
					H
					N
					E
					Y
					P
					Y
					T
					F
					G
					702
GGG CGG ACC AAG CTT GAG ATC AAA 3'					

G	G	T	K	L	E
					I
					K

Figure 6.6

25/40

9	18	27	36	45	54												
GAG	GTG	CAG	CTG	CTC	GAG	CAG	TCT	GGA	CCT	GAG	CTG	GTA	AGG	CCT	GGG	ACT	TCA
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E	V	Q	L	L	E	Q	S	G	A	E	L	V	R	P	G	T	S
63					72			81			90			99			108
GTG	AAG	ATA	TCC	TGC	AAG	GCT	TCT	GGA	TAC	GCC	TTC	ACT	AAC	TAC	TGG	CTA	GGT
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
V	K	I	S	C	K	A	S	G	Y	A	F	T	N	Y	W	L	G
117					126			135			144			153			162
TGG	GTT	AAG	CAG	AGG	CCT	GGA	CAT	GGA	CTT	GAA	TGG	GTT	GGA	GAT	ATT	TTC	CCT
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
W	V	K	Q	R	P	G	H	G	L	E	W	V	G	D	I	F	P
171					180			189			198			207			216
GGA	AGT	GGT	AAT	GCT	CAC	TAC	AAT	GAG	AAG	TTC	AAG	GGC	AAA	GCC	ACA	CTG	ACT
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
G	S	G	N	A	H	Y	N	E	K	F	K	G	K	A	T	L	T
225					234			243			252			261			270
GCA	GAC	AAG	TCC	TCG	TAC	ACA	GCC	TAT	ATG	CAG	CTC	AGT	AGC	CTG	ACA	TCT	GAG
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
A	D	K	S	S	Y	T	A	Y	M	Q	L	S	S	L	T	S	E
279					288			297			306			315			324
GAC	TCT	GCT	GTC	TAT	TTC	TGT	GCA	AGA	TTG	CGG	AAC	TGG	GAC	GAG	GCT	ATG	GAC
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
D	S	A	V	Y	F	C	A	R	L	R	N	W	D	E	A	M	D
333					342			351			360			369			378
TAC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT	GGT	GGT	TCT	GGC
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Y	W	G	Q	G	T	T	V	T	V	S	S	G	G	G	G	S	G
387					396			405			414			423			432
GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	GAG	CTC	GTG	ATG	ACA	CAG	TCT	CCA	TCC
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
G	G	G	S	G	G	G	S	E	L	V	M	T	Q	S	P	S	
441					450			459			468			477			486
TCC	CTG	AGT	GTG	TCA	GCA	GGA	GAG	AAG	GTC	ACT	ATG	AGC	TGC	AAG	TCC	AGT	CAG
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
S	L	S	V	S	A	G	E	K	V	T	M	S	C	K	S	S	Q
495					504			513			522			531			540
AGT	CTG	TTA	AAC	AGT	GGA	AAT	CAA	AAG	AAC	TAC	TTG	GCC	TGG	TAC	CAG	CAG	AAA
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
S	L	L	N	S	G	N	Q	K	N	Y	L	A	W	Y	Q	Q	K
549					558			567			576			585			594
CCA	GGG	CAG	CCT	CCT	AAA	CTG	TTG	ATC	TAC	GGG	GCA	TCC	ACT	AGG	GAA	TCT	GGG
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
P	G	Q	P	P	K	L	L	I	Y	G	A	S	T	R	E	S	G
603					612			621			630			639			648
GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GGA	ACA	GAT	TTC	ACT	CTC	ACC	ATC
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I
657					666			675			684			693			702
AGC	AGT	GTG	CAG	GCT	GAA	GAC	CTG	GCA	GTT	TAT	TAC	TGT	CAG	AAT	GAT	TAT	AGT
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
S	S	V	Q	A	E	D	L	A	V	Y	Y	C	Q	N	D	Y	S
711					720			729			738						
TAT	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG	CTT	GAG	ATC	AAA	-3'			
-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Y	P	Y	T	F	G	G	G	T	K	L	E	I	K				

Figure 6.7

26 / 40

Figure 6.8

27/40

5'	y	18	27	36	45	54												
	GAG	GTG	CAG	CTG	CTC	GAG	CAG	TCT	GGA	GCT	GAG	CTG	GCG	AGG	CCT	GGG	GCT	TCA
	E	V	Q	L	L	E	Q	S	G	A	E	L	A	R	P	G	A	S
	63					72			81			90			99			108
	GTG	AAG	CTG	TCC	TGC	AAG	GCT	TCT	GGC	TAC	ACC	TTC	ACA	AAC	TAT	GGT	TTA	AGC
	V	K	L	S	C	K	A	S	G	Y	T	F	T	N	Y	G	L	S
	117					126			135			144			153			162
	TGG	GTG	AAG	CAG	AGG	CCT	GGA	CAG	GTC	CTT	GAG	TGG	ATT	GGA	GAG	GTT	TAT	CCT
	W	V	K	Q	R	P	G	Q	V	L	E	W	I	G	E	V	Y	P
	171					180			189			198			207			216
	AGA	ATT	GGT	AAT	GCT	TAC	TAC	AAT	GAG	AAG	TTC	AAG	GGC	AAG	GCC	ACA	CTG	ACT
	R	I	G	N	A	Y	Y	N	E	K	F	K	G	K	A	T	L	T
	225					234			243			252			261			270
	GCA	GAC	AAA	TCC	TCC	AGC	ACA	GCG	TCC	ATG	GAG	CTC	CGC	AGC	CTG	ACC	TCT	GAG
	A	D	K	S	S	S	T	A	S	M	E	L	R	S	L	T	S	E
	279			288				297			306			315			324	
	GAC	TCT	GCG	GTC	TAT	TTC	TGT	GCA	AGA	CGG	GGA	TCC	TAC	GAT	ACT	AAC	TAC	GAC
	D	S	A	V	Y	F	C	A	R	R	G	S	Y	D	T	N	Y	D
	333					342			351			360			369			378
	TGG	TAC	TTC	GAT	GTC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT
	W	Y	F	D	V	W	G	Q	G	T	T	V	T	V	S	S	G	G
	387					396			405			414			423			432
	GGT	GGT	TCT	GGC	GGC	GGC	TCC	GGT	GGT	GGT	GGT	TCT	GAG	CTC	GTG	ATG	ACC	
	G	G	S	G	G	G	S	G	G	G	G	S	E	L	V	M	T	
	441			450				459			468			477			486	
	CAG	ACT	CCA	CTC	TCC	CTG	CCT	GTC	AGT	CTT	GGA	GAT	CAA	GCC	TCC	ATC	TCT	TGC
	Q	T	P	L	S	L	P	V	S	L	G	D	Q	A	S	I	S	C
	495				504				513			522			531			540
	AGA	TCT	AGT	CAG	AGC	CTT	GTA	CAC	AGT	AAT	GGA	AAC	ACC	TAT	TTA	CAT	TGG	TAC
	R	S	S	Q	S	L	V	H	S	N	G	N	T	Y	L	H	W	Y
	549					558			567			576			585			594
	CTG	CAG	AAG	CCA	GGC	CAG	TCT	CCA	AAG	CTC	CTG	ATC	TAC	AAA	GGT	TCC	AAC	CGA
	L	Q	K	P	G	Q	S	P	K	L	L	I	Y	K	V	S	N	R
	603					612			621			630			639			648
	TTT	TCT	GGG	GTC	CCA	GAC	AGG	TTC	AGT	GGC	AGT	GGA	TCA	GGG	ACA	GAT	TTC	ACA
	F	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T
	657					666			675			684			693			702
	CTC	AAG	ATC	AGC	AGA	GTG	GAG	GCT	GAG	GAT	CTG	GGA	GTT	TAT	TTC	TGC	TCT	CAA
	L	K	I	S	R	V	E	A	E	D	L	G	V	Y	F	C	S	Q
	711					720			729			738			747			
	AGT	ACA	CAT	GTT	CCG	TAC	ACG	TTC	GGA	GGG	GGG	ACC	AAG	CTT	GAG	ATC	AAA	3'
	S	T	H	V	P	Y	T	F	G	G	G	T	K	L	E	I	K	

Figure 6.9

28/40

	9	18	27	36	45	54													
5'	GAG	GTG	CAG	CTG	CTC	GAG	TCT	GGA	GGT	GGC	CTG	GTG	CAG	CCT	GGA	GGA	TCC	CTG	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	E	V	Q	L	L	E	S	G	G	G	L	V	Q	P	G	G	S	L	
	63					72					81			90			99		108
	AAA	CTC	TCC	TGT	GCA	GCC	TCA	GGA	TTC	GAT	TTT	AGT	AGA	TAC	TGG	ATG	AGT	TGG	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	K	L	S	C	A	A	S	G	F	D	F	S	R	Y	W	M	S	W	
	117					126			135			144			153			162	
	GTC	CGG	CAG	GCT	CCA	GGG	AAA	GGG	CTA	GAA	TGG	ATT	GGA	GAA	ATT	AAT	CCA	GAT	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	V	R	Q	A	P	G	K	G	L	E	W	I	G	E	I	I	N	P	D
	171				180				189			198			207			216	
	AGC	AGT	ACG	ATA	AAC	TAT	ACG	CCA	TCT	CTG	AAG	GAT	AAA	TTC	ATC	ATC	TCC	AGA	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	S	S	T	I	N	Y	T	P	S	L	K	D	K	F	I	I	S	R	
	225				234				243			252			261			270	
	GAC	AAC	GCC	AAA	AAT	ACG	CTG	TAC	CTG	CAA	ATG	GGC	AAA	GTG	AGA	TCT	GAG	GAC	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	D	N	A	K	N	T	L	Y	L	Q	M	G	K	V	R	S	E	D	
	279				288				297			306			315			324	
	ACA	GCC	CTT	TAT	TAC	TGT	GCA	AGA	GGA	GCC	TTC	CTT	TTT	GAC	TAC	TGG	GGC	CAA	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	T	A	L	Y	Y	C	A	R	G	A	F	L	F	D	Y	W	G	Q	
	333				342				351			360			369			378	
	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT	GGT	GGT	TCT	GGC	GGC	GGC	GGC	TCC	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	G	T	T	V	T	V	S	S	G	G	G	G	S	G	G	G	G	S	
	387				396				405			414			423			432	
	GGT	GGT	GGT	TCT	GAG	CTC	GTG	CTC	ACC	CAG	TCT	CCA	ACC	ACC	ATG	GCT	GCA		
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	G	G	G	G	S	E	L	V	L	T	Q	S	P	T	T	M	A	A	
	441				450				459			468			477			486	
	TCT	CCC	GGG	GAG	AAG	ATC	ACT	ATC	ACC	TGC	AGT	GCC	AGC	TCA	AGT	ATA	AGT	TCC	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	S	P	G	E	K	I	T	I	T	C	S	A	S	S	S	I	S	S	
	495				504				513			522			531			540	
	AAT	TAC	TTG	CAT	TGG	TAT	CAG	CAG	AAG	CCA	GGA	TTC	TCC	CCT	AAA	CTC	TTG	ATT	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	N	Y	L	H	W	Y	Q	Q	K	P	G	F	S	P	K	L	L	I	
	549				558				567			576			585			594	
	TAT	AGG	ACA	TCC	AAT	CTG	GCT	TCT	GGA	GTC	CCA	GCT	CGC	TTC	AGT	GGC	AGT	GGG	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	Y	R	T	S	N	L	A	S	G	V	P	A	R	F	S	G	S	G	
	603				612				621			630			639			648	
	TCT	GGG	ACC	TCT	TAC	TCT	CTC	ACA	ATT	GGC	ACC	ATG	GAG	GCT	GAA	GAT	GTT	GCC	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	S	G	T	S	Y	S	L	T	I	G	T	M	E	A	E	D	V	A	
	657				666				675			684			693			702	
	ACT	TAC	TAC	TGC	CAG	CAG	GGT	AGT	AGT	ATA	CCA	CTC	ACG	TTC	GGT	GCT	GGG	ACC	
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
	T	Y	Y	C	Q	Q	G	S	S	I	P	L	T	F	G	A	G	T	
	711																		
	AAG	CTT	GAG	ATC	AAA	3'													
	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
	K	L	E	I	K														

Figure 6.10

29/40

9	18	27	36	45	54												
GAG	GTG	CAG	CTG	CTC	GAG	CAG	TCT	GGA	GCT	GAG	CTG	GTA	AGG	CCT	GGG	ACT	TCA
E	V	Q	L	L	E	Q	S	G	A	E	L	V	R	P	G	T	S
63					72			81			90			99			108
GTG	AAG	ATA	TCC	TGC	AAG	GCT	TCT	GGA	TAC	GCC	TTC	ACT	AAC	TAC	TGG	CTA	GGT
V	K	I	S	C	K	A	S	G	Y	A	F	T	N	Y	W	L	G
117					126			135			144			153			162
TGG	GTA	AAG	CAG	AGG	CCT	GGA	CAT	GGA	CTT	GAG	TGG	ATT	GGA	GAT	ATT	TTC	CCT
W	V	K	Q	R	P	G	H	G	L	E	W	I	G	D	I	F	P
171					180			189			198			207			216
GGA	AGT	GGT	AAT	ATC	CAC	TAC	AAT	GAG	AAG	TTC	AAG	GGC	AAA	GCC	ACA	CTG	ACT
G	S	G	N	I	H	Y	N	E	K	F	K	G	K	A	T	L	T
225					234			243			252			261			270
GCA	GAC	AAA	TCT	TCG	AGC	ACA	GCC	TAT	ATG	CAG	CTC	AGT	AGC	CTG	ACA	TTT	GAG
A	D	K	S	S	S	T	A	Y	M	Q	L	S	S	L	T	F	E
279					288			297			306			315			324
GAC	TCT	GCT	GTC	TAT	TTC	TGT	GCA	AGA	CTG	AGG	AAC	TGG	GAC	GAG	CCT	ATG	GAC
D	S	A	V	Y	F	C	A	R	L	R	N	W	D	E	P	M	D
333					342			351			360			369			378
TAC	TGG	GGC	CAA	GGG	ACC	ACG	GTC	ACC	GTC	TCC	TCA	GGT	GGT	GGT	GGT	TCT	GGC
Y	W	G	Q	G	T	T	V	T	V	S	S	G	G	G	G	S	G
387					396			405			414			423			432
GGC	GGC	GGC	TCC	GGT	GGT	GGT	TCT	GAG	CTC	GTG	ATG	ACA	CAG	TCT	CCA	TCC	
G	G	G	S	G	G	G	S	E	L	V	M	T	Q	S	P	S	
441					450			459			468			477			486
TCC	CTG	ACT	GTG	ACA	GCA	GGA	GAG	AAG	GTC	ACT	ATG	AGC	TGC	AAG	TCC	AGT	CAG
S	L	T	V	T	A	G	E	K	V	T	M	S	C	K	S	S	Q
495					504			513			522			531			540
AGT	CTG	TTA	AAC	AGT	GGG	AAT	CAA	AAG	AAC	TAC	TTG	ACC	TGG	TAC	CAG	CAG	AAA
S	L	L	N	S	G	N	Q	K	N	Y	L	T	W	Y	Q	Q	K
549					558			567			576			585			594
CCA	GGG	CAG	CCT	CCT	AAA	CTG	TTG	ATC	TAC	TGG	GCA	TCC	ACT	AGG	GAA	TCT	GGG
P	G	Q	P	P	K	L	L	I	Y	W	A	S	T	R	E	S	G
603					612			621			630			639			648
GTC	CCT	GAT	CGC	TTC	ACA	GGC	AGT	GGA	TCT	GGA	ACA	GAT	TTC	ACT	CTC	ACC	ATC
V	P	D	R	F	T	G	S	G	S	G	T	D	F	T	L	T	I
657					666			675			684			693			702
AGC	AGT	GTG	CAG	GCT	GAA	GAC	CTG	GCA	GTG	TAT	TAC	TGT	CAG	AAT	GAT	TAT	AGT
S	S	V	Q	A	E	D	L	A	V	Y	Y	C	Q	N	D	Y	S
711					720			729			738						
TAT	CCG	CTC	ACG	TTC	GGT	GCT	GGG	ACC	AAG	CTT	GAG	ATC	AAA	3'			
Y	P	L	T	F	G	A	G	T	K	L	E	I	K				

Figure 7

30/40

	9	18	27	36	45	54
5'	GAG GTG CAG CTG CTC GAG CAG TCT GGA GCT GAG CTG GTA AGG CCT GGG ACT TCA					
	-----	-----	-----	-----	-----	-----
	E V Q L L E Q S G A E L V R P G T S					
	63 72 81 90 99 108					
	GTG AAG ATA TCC TGC AAG GCT TCT GGA TAC GCC TTC ACT AAC TAC TGG CTA GGT					
	-----	-----	-----	-----	-----	-----
	V K I S C K A S G Y A F T N Y W L G					
	117 126 135 144 153 162					
	TGG GTT AAG CAG AGG CCT GGA CAT GGA CTT GAA TGG GTT GGA GAT ATT TTC CCT					
	-----	-----	-----	-----	-----	-----
	W V K Q R P G H G L E W V G D I F P					
	171 180 189 198 207 216					
	GGA AGT GGT AAT GCT CAC TAC AAT GAG AAG TTC AAG GGC AAA GCC ACA CTG ACT					
	-----	-----	-----	-----	-----	-----
	G S G N A H Y N E K F K G K A T L T					
	225 234 243 252 261 270					
	GCA GAC AAG TCC TCG TAC ACA GCC TAT ATG CAG CTC AGT AGC CTG ACA TCT GAG					
	-----	-----	-----	-----	-----	-----
	A D K S S Y T A Y M Q L S S L T S E					
	279 288 297 306 315 324					
	GAC TCT GCT GTC TAT TTC TGT GCA AGA TTG CGG AAC TGG GAC GAG GCT ATG GAC					
	-----	-----	-----	-----	-----	-----
	D S A V Y F C A R L R N W D E A M D					
	333 342 351 360 369 378					
	TAC TGG GGC CAA GGG ACC ACG GTC ACC GTC TCC TCA GGT GGT GGT GGT TCT GGC					
	-----	-----	-----	-----	-----	-----
	Y W G Q G T T V T V S S G G G S G					
	387 396 405 414 423 432					
	GGC GGC GGC TCC GGT GGT GGT TCT GAG CTC GTG ATG ACA CAG TCT CCA TCC					
	-----	-----	-----	-----	-----	-----
	G G G S G G G S E L V M T Q S P S					
	441 450 459 468 477 486					
	TCC CTG GCT ATG TCA GTA GGA CAG AAG GTC ACT ATG AGC TGC AAG TCC AGT CAG					
	-----	-----	-----	-----	-----	-----
	S L A M S V G Q K V T M S C K S S Q					
	495 504 513 522 531 540					
	AGC CTT TTA AAT AGT AGC AAT CAA AAG AAC TAT TTG GCC TGG TAC CAG CAG AAA					
	-----	-----	-----	-----	-----	-----
	S L L N S S N Q K N Y L A W Y Q Q K					
	549 558 567 576 585 594					
	CAA GGG CAG CCT CCT AAA CTG CTT ATC TAT GGG GCA TCC ATT AGA GAA TCT TGG					
	-----	-----	-----	-----	-----	-----
	Q G Q P P K L L I Y G A S I R E S W					
	603 612 621 630 639 648					
	GTC CCT GAT CGA TTC ACA GGA AGT GGA TCT GGG ACA GAC TTC ACT CTC ACC ATC					
	-----	-----	-----	-----	-----	-----
	V P D R F T G S G S G T D F T L T I					
	657 666 675 684 693 702					
	AGC AGT GTG AAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA TAT TAT AGC					
	-----	-----	-----	-----	-----	-----
	S S V K A E D L A V Y Y C Q Q Y Y Y S					
	711 720 729 738					
	TAT CCG TAC ACG TTC GGA GGG ACC AAG CTT GAG ATC AAA 3'					
	-----	-----	-----	-----	-----	-----
	Y P Y T F G G T K L E I K					

Figure 8.1

ELISA -analysis
CD 80-Anti-17-1A scFv 3-1 - 5-13 (PS)
Detection: anti - CD 80

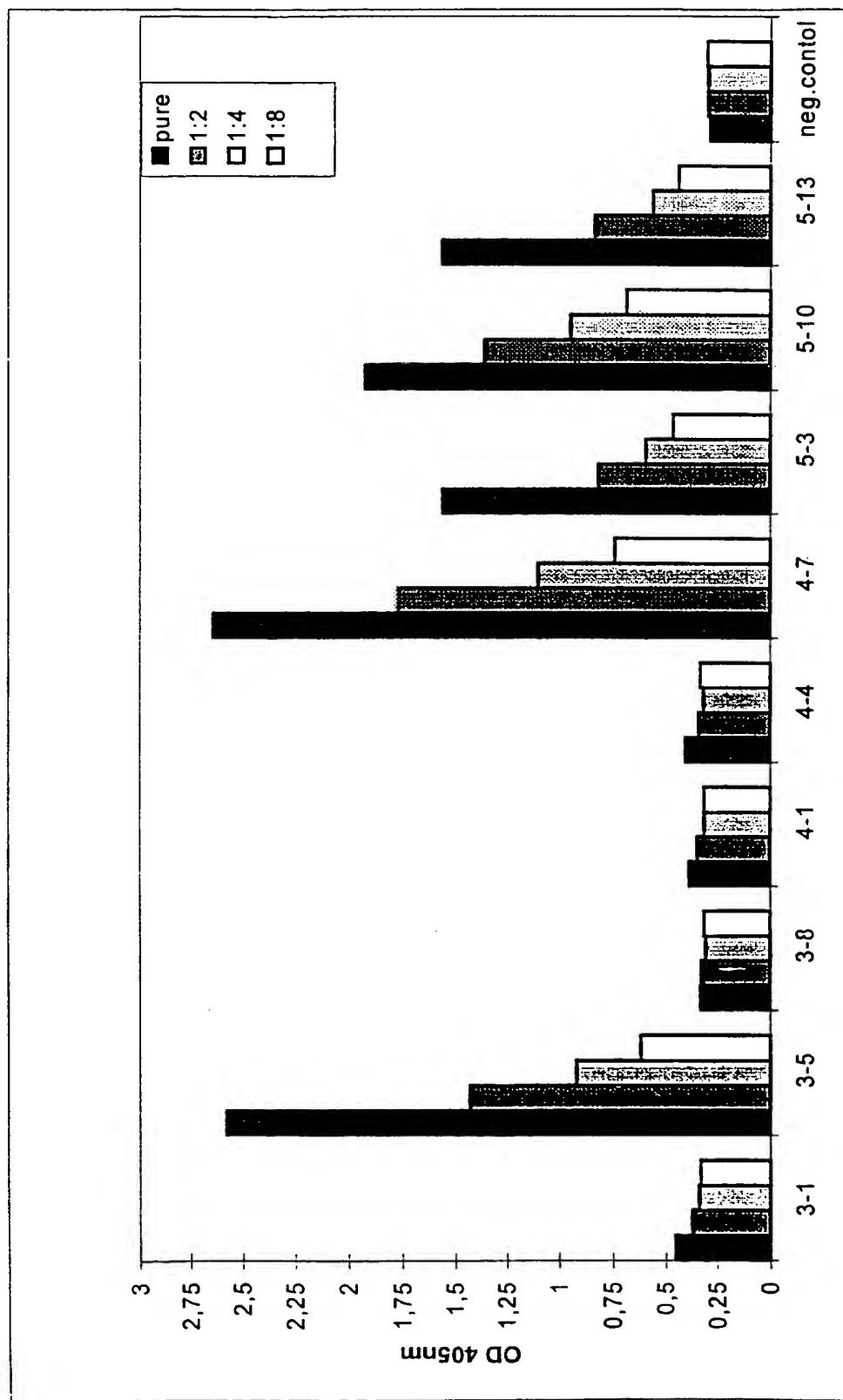


Figure 8.2

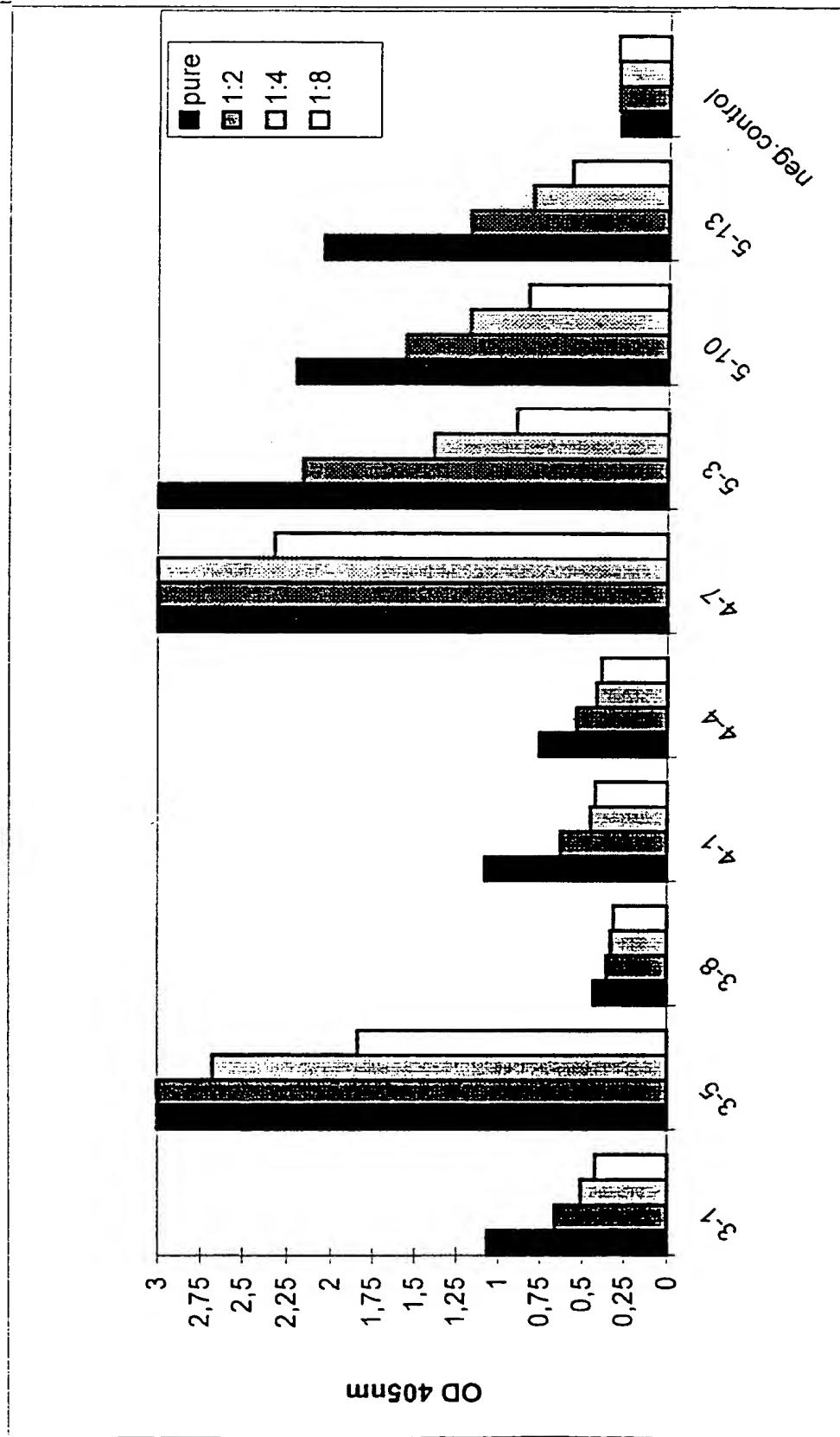
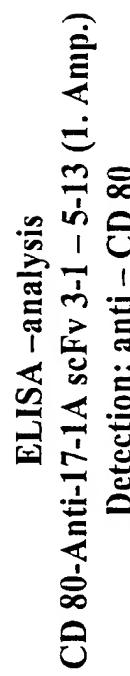


Figure 8.3

ELISA -analysis
CD 80-VD4.5V_k8 scFv (PS) and CD 80-Mach scFv (PS)
Detection: anti - CD 80

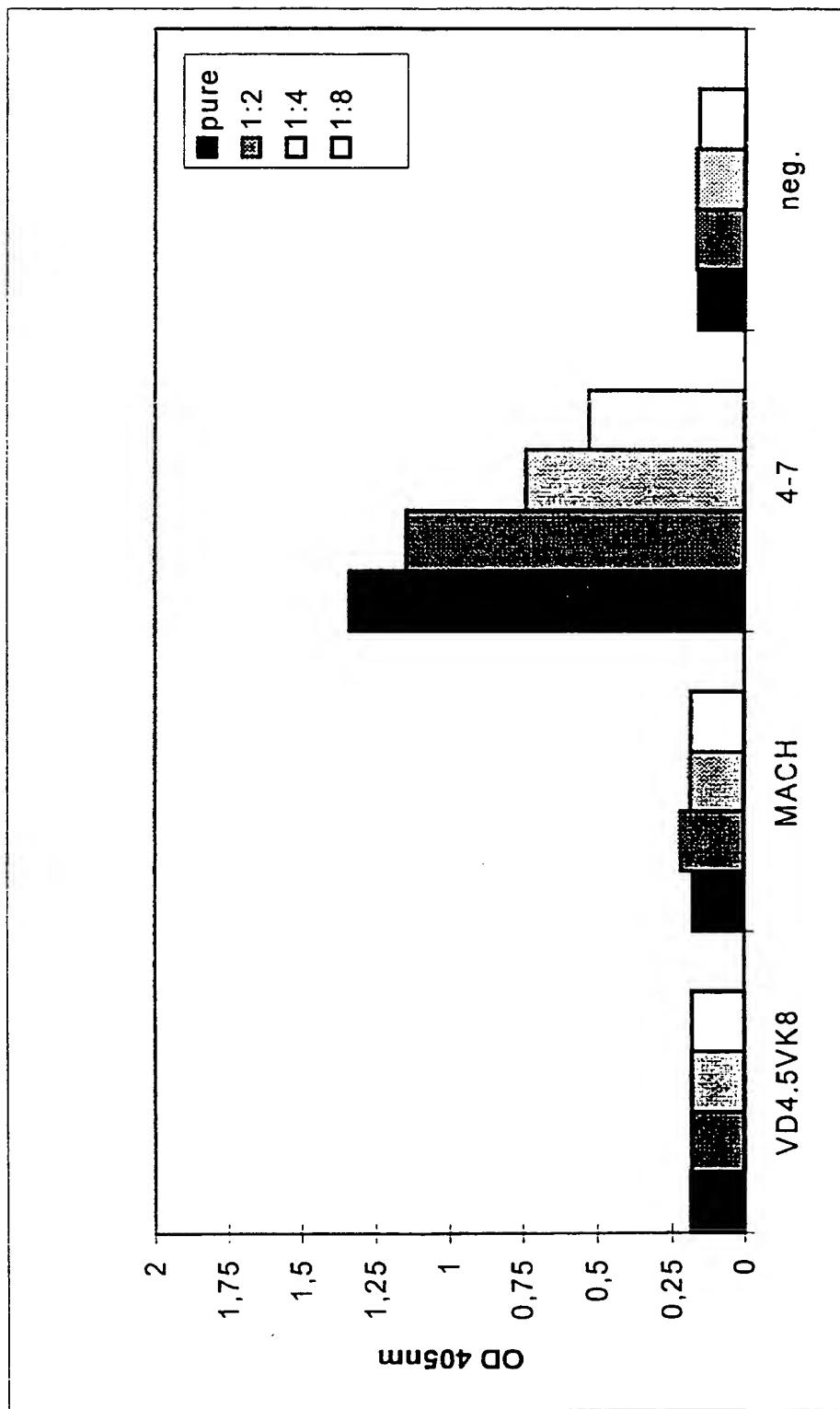


Figure 8.4

ELISA -analysis
CD 80-VD4.5Vdk8 scFv (1. Amp.) and CD 80-Mach scFv (1. Amp.)
Detection: anti - CD 80

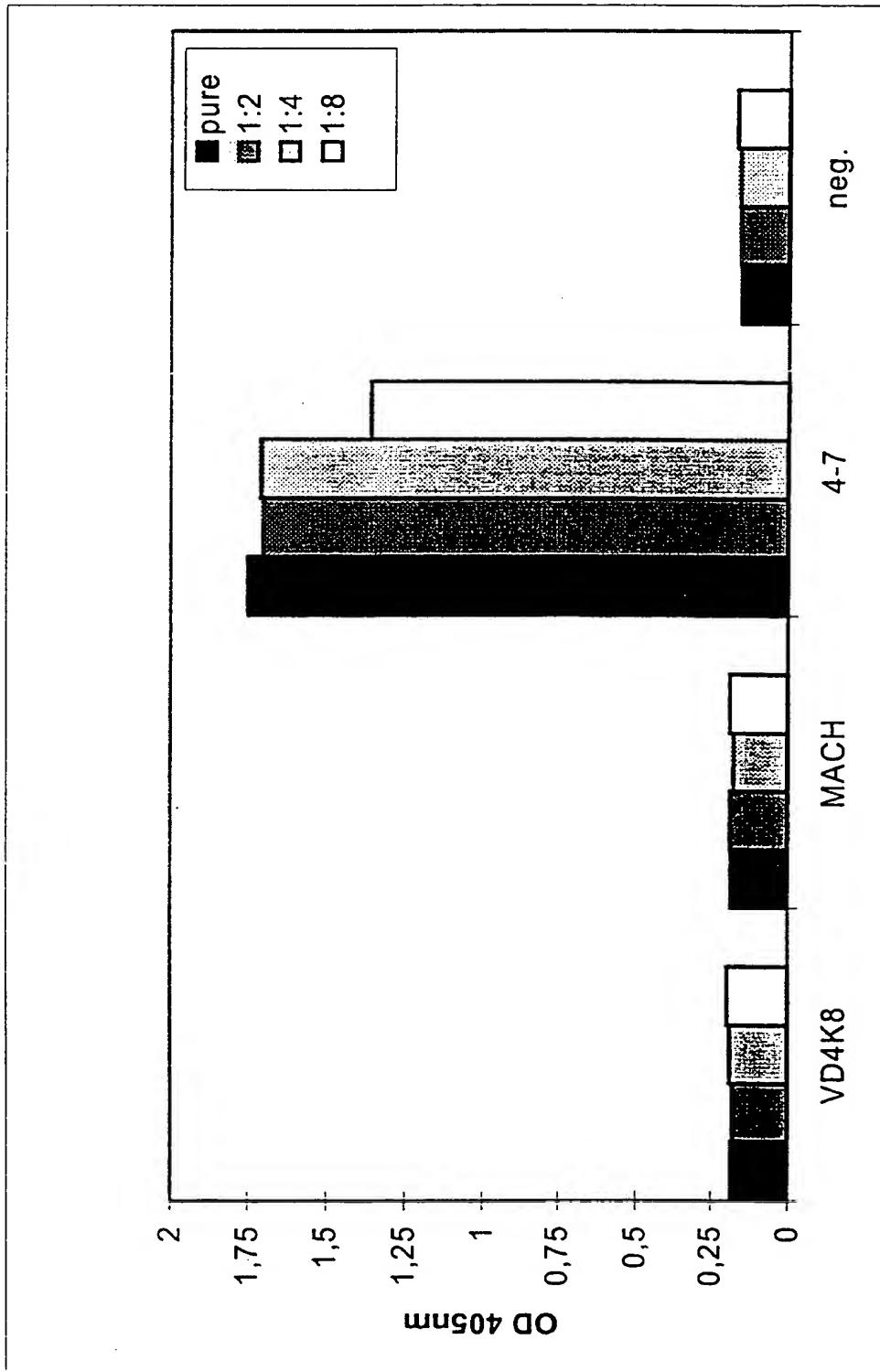


Figure 9.1

Part 1

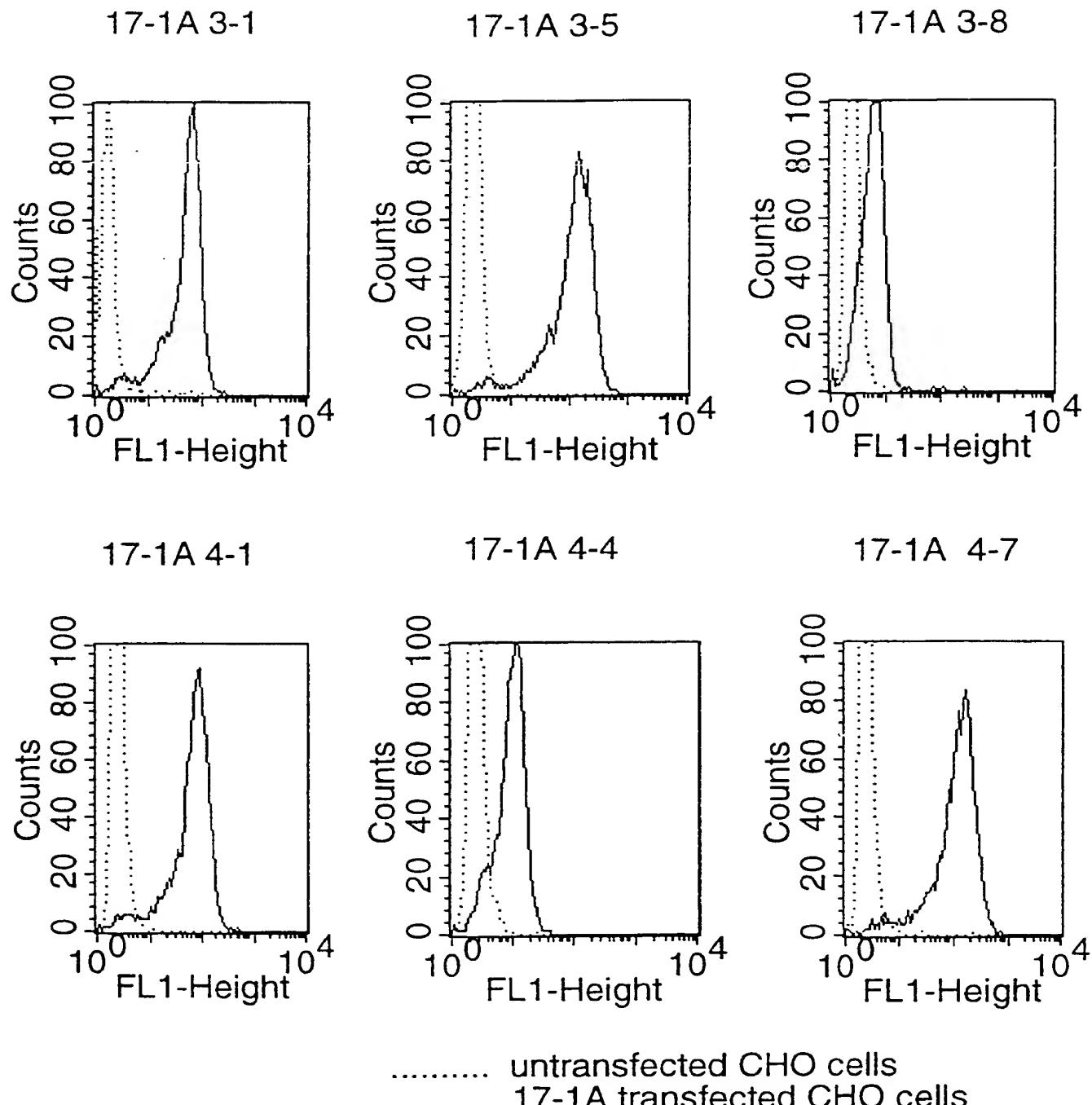


Figure 9.1

Part 2

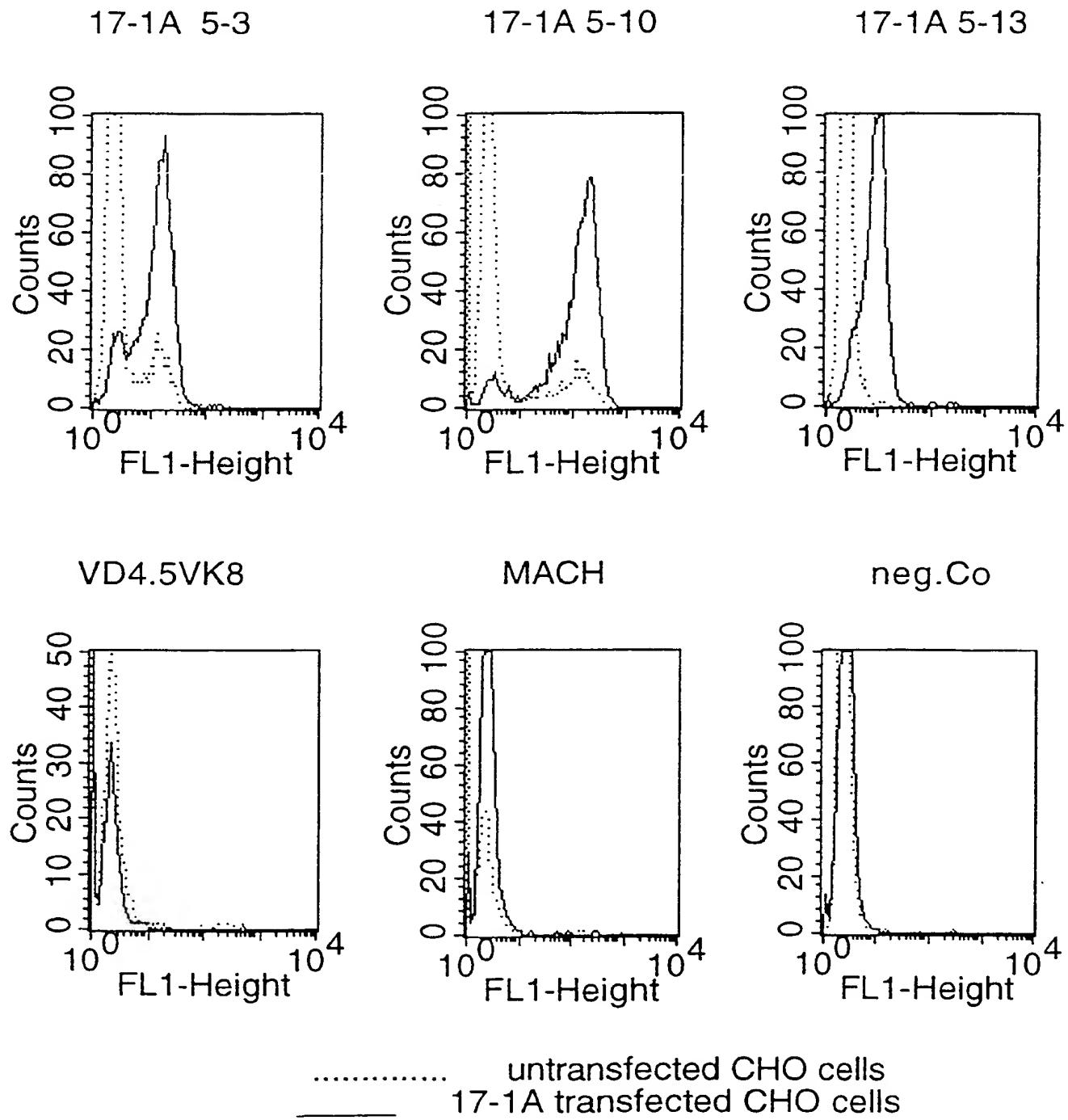


Figure 9.2

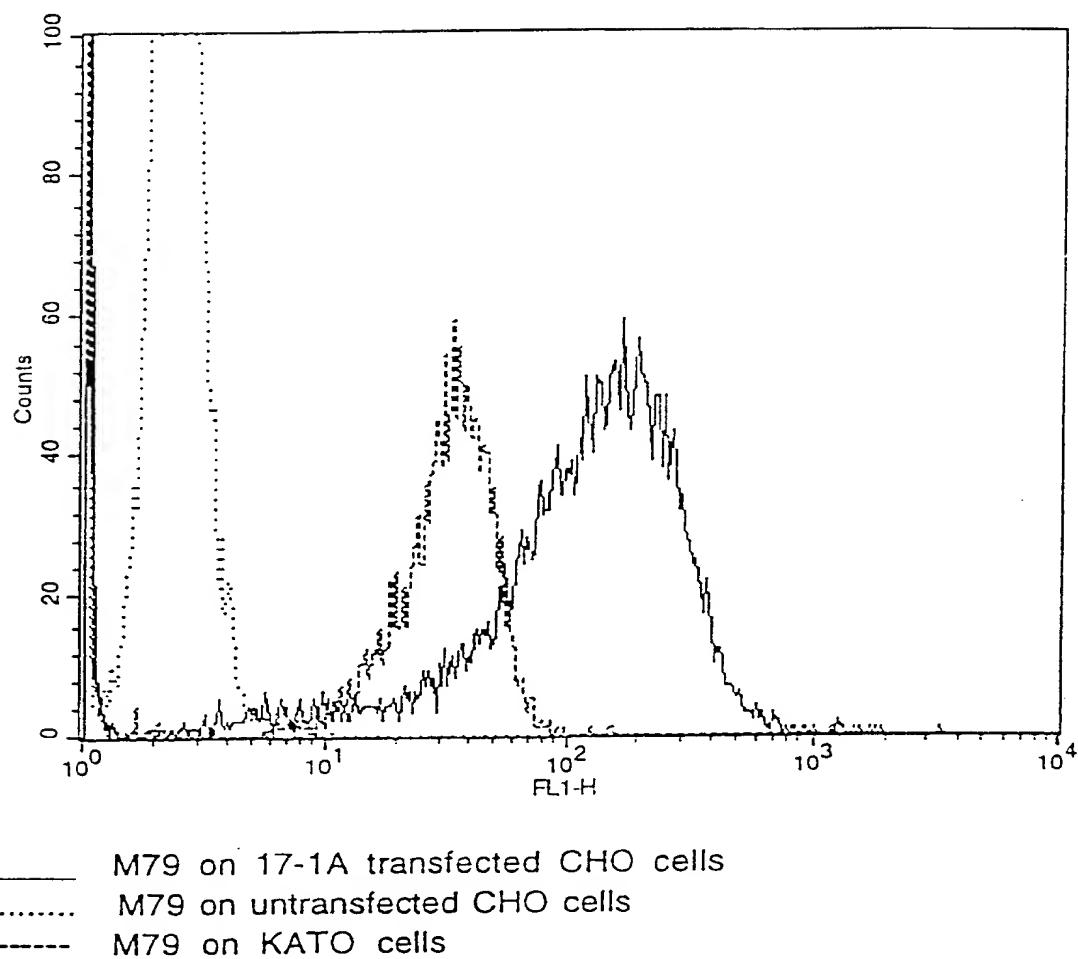
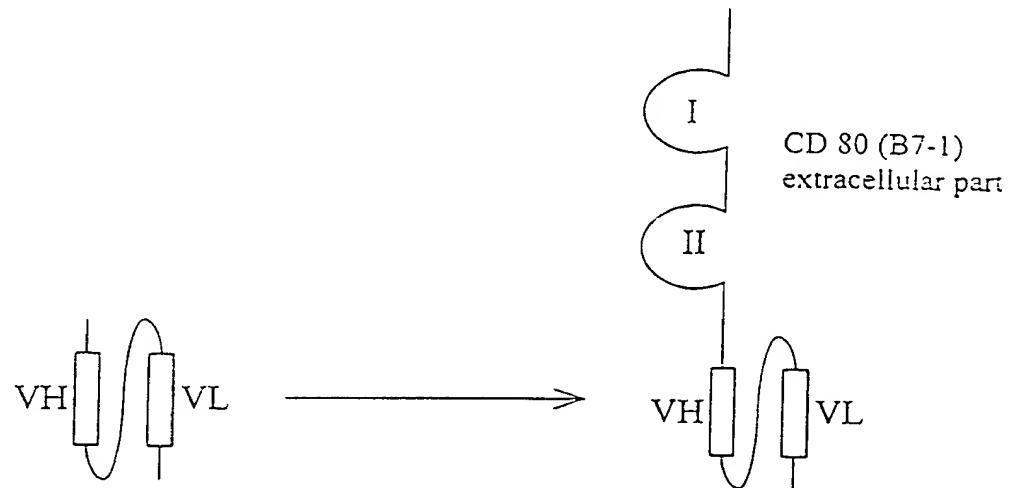


Figure 10

1) The Conventional approach

Randomly selected antigen-specific VH/VL-pairs that bind to their antigen as free or N-terminally located scFv-fragments or as whole antibody molecules

Frequent loss of antigen binding after fusion of another protein domain to the N-terminus of the scFv-fragment



2) The method of invention

VH/VL-pairs selected by the method of the invention

High frequency of antigen binding after fusion of another protein domain to the N-terminus of the scFv-fragment

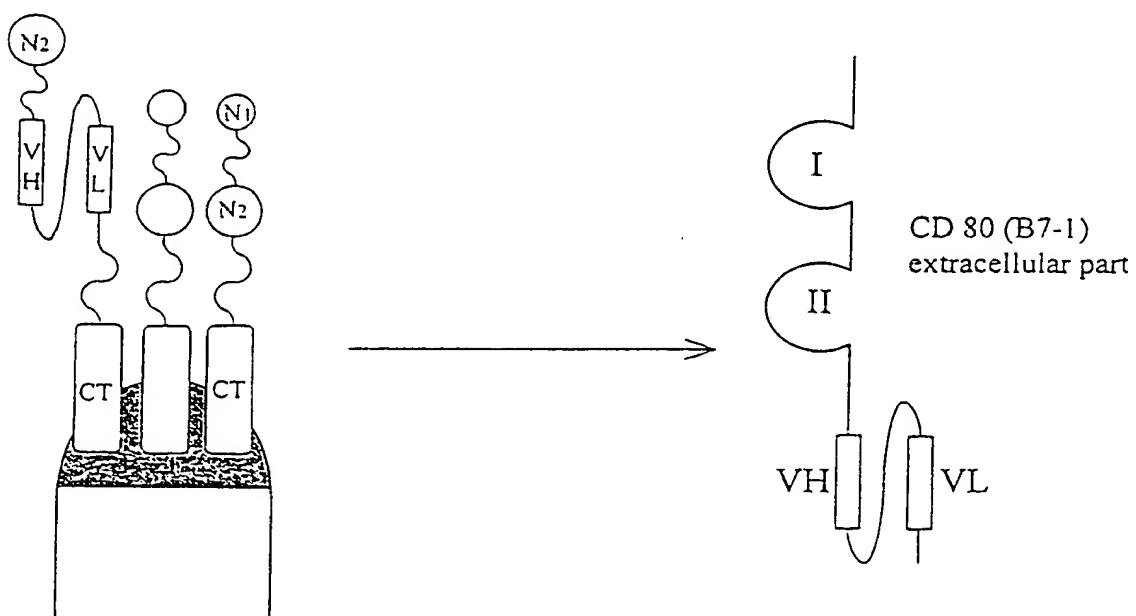


Figure 11

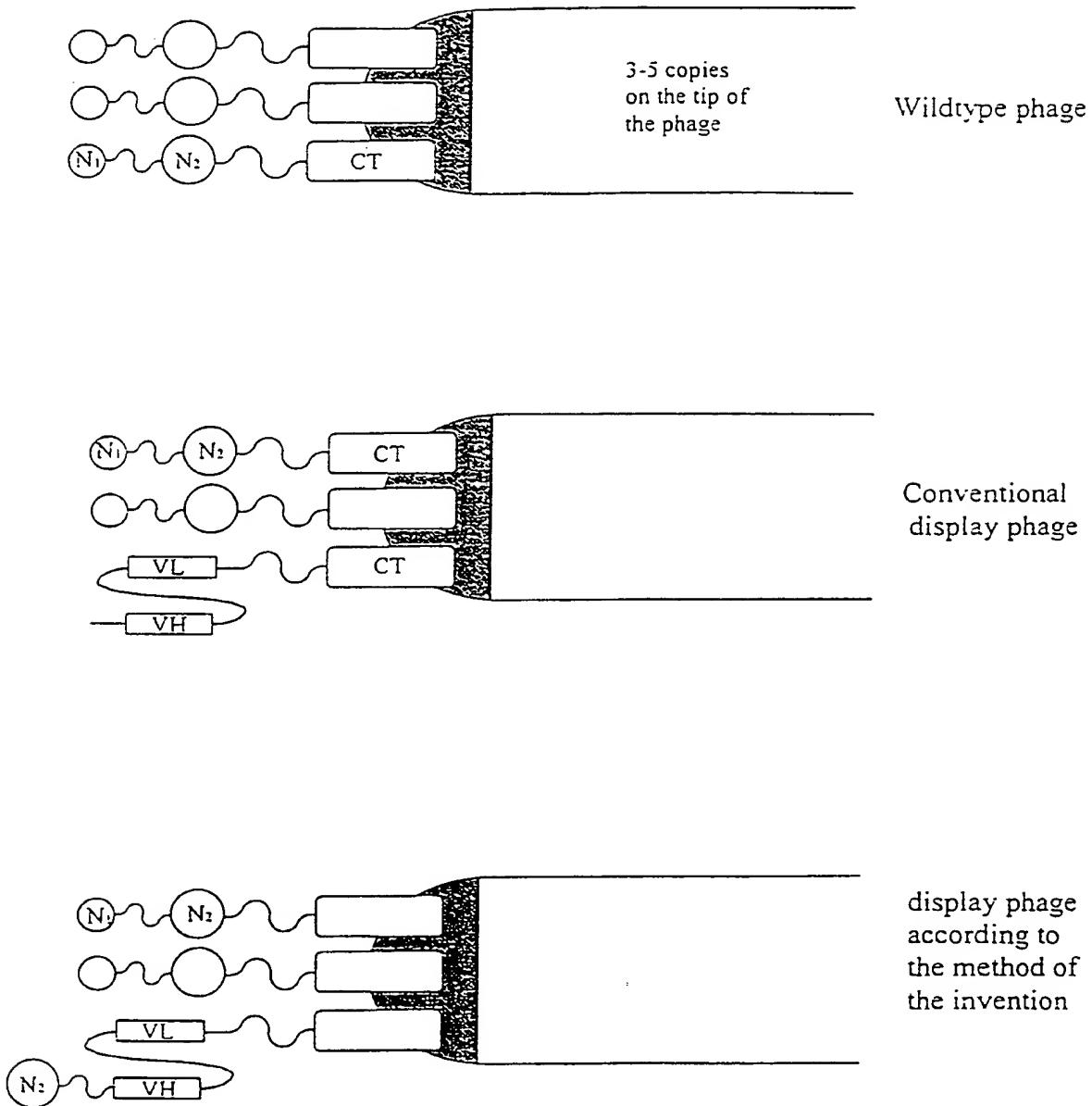


Figure 12

ELISA on different anti 17-1A-CD54, anti 17-1A CD58, anti 17-1A

CD86 constructs

